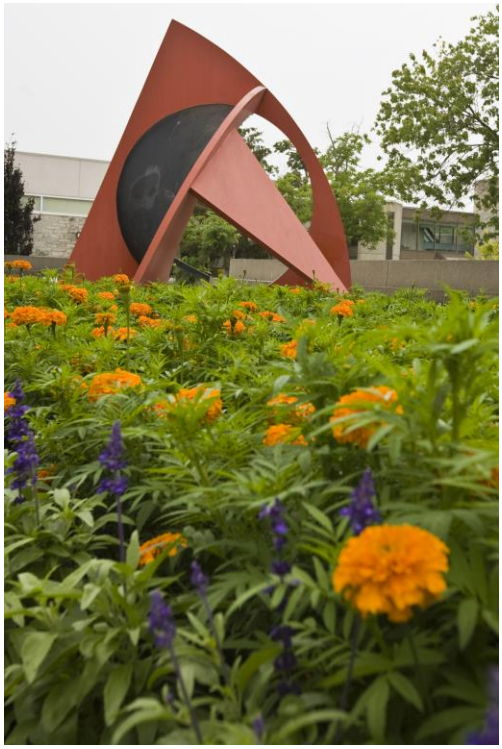
The Twenty-First Annual Scientific Meeting for Health Science Research Trainees
Faculty of Health Sciences
Queen's University

Wednesday, June 13th, 2018
Biosciences Complex



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Acknowledgments

A special thank you to Katherine Brennan-Rowcliffe for her invaluable assistance in organizing this meeting.

The Twenty-First Annual Scientific Meeting for Health Science Research Trainees

Faculty of Health Sciences

Queen's University

Wednesday, June 13th, 2018

Biosciences Complex, Atrium and School of Medicine

Wednesday, June 13th, 2018

Poster Presentations taking place in Biosciences Complex, Atrium

Oral Presentations taking place in School of Medicine Building, Room 132A

8:00 – 8:45 ***Registration and Poster Set-Up in Biosciences Complex, Atrium***

8:45 – 9:00 ***Introductory Remarks Rm 132A, School of Medicine Building***
Dr. Brian Bennett, Associate Dean, Graduate and Postdoctoral Education, Faculty of Health Sciences
Dr. Christopher Simpson, Acting Dean, Faculty of Health Sciences

9:00 – 9:30 ***Keynote Speaker***
Dr. Anne Ellis
Departments of Medicine and Biomedical & Molecular Sciences
"Deconstrucing Allergy: From its Developmental Origins to its Pathophysiology to New Therapies and Prevention"

Oral Presentation – Session 1

Chair: Dr. Madhuri Koti

9:35 – 9:47 Jeff M. Mah - **ASSOCIATION BETWEEN HOSPITAL TEACHING STATUS AND SURVIVAL FOLLOWING TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS): A POPULATION-BASED STUDY**

9:47 – 9:59 Kayla Colledanchise - **FEMORAL PLAQUE QUANTIFICATION FOR THE PREDICTION OF CORONARY ARTERY DISEASE IN MEN AND WOMEN**

9:59 – 10:11 Jennifer Carroll - **CULTURAL HUMILITY AND TRANSGENDER CLIENTS: A STUDY EXAMINING THE RELATIONSHIP BETWEEN CRITICAL REFLECTION AND ATTITUDES OF NURSE PRACTITIONERS**

10:11 – 10:23 Jesse Leblanc - **TCF3-PBX1 ACTIVATES PROLIFERATION-PROMOTING SIGNALING PATHWAYS INDEPENDENT OF THE PRE-B-CELL RECEPTOR IN ACUTE LYMPHOBLASTIC LEUKEMIA**

10:25 – 10:45 ***Coffee Break (Biosciences Atrium)***

10:45 – 12:15 Poster Presentations (Odd Numbered Abstracts)

12:15 – 1:00 Lunch

1:00 – 2:30 Poster Presentations (Even Numbered Abstracts)

Oral Presentation – Session 2

Chair: Dr. Mark Ormiston

2:30 – 2:42 Natalya Odoardi - **INTERLEUKIN-27 DIFFERENTIALLY MODULATES TOLL-LIKE RECEPTOR 7 AND 8 FUNCTION IN HUMAN MONOCYTES AND MACROPHAGES**

2:42 – 2:54 Philip Zakas - **MOLECULAR CO-EVOLUTION OF COAGULATION FACTOR VIII AND VON WILLEBRAND FACTOR**

2:54 – 3:06 Vanessa Kay - **INTERVENING IN THE POSTNATAL PERIOD IN A MOUSE MODEL OF PREECLAMPSIA-INDUCED OFFSPRING COGNITIVE AND NEUROANATOMICAL ALTERATIONS**

3:06 – 3:18 Anne Theilmann - **SUB-HAPLOINSUFFICIENCY OF *BMPR2* CAUSES A SHIFT IN THE ENDOTHELIAL PROLIFERATIVE AND METABOLIC RESPONSE TO BMP9**

3:18– 3:30 Byron Hunter - **DEFINING THE MOLECULAR BASIS OF MICROTUBULE LENGTH REGULATION IN CANDIDA ALBICANS**

3:30 – 3:45 ***Coffee Break (School of Medicine Building, Atrium)***

Oral Presentation – Session 3

Chair: Dr. Stephan Pang

3:45 – 3:57 Emma Robertson - **CEREBROSPINAL FLUID BIOMARKERS IN A NONHUMAN PRIMATE MODEL OF ALZHEIMER'S DISEASE**

3:57 – 4:09 Nicole Morse - **A MASS SPECTROMETRY IMAGING-BASED CLASSIFIER IDENTIFIES THE IMPORTANCE OF DYSREGULATED METABOLISM IN PROSTATE CANCER DIAGNOSIS**

4:09 – 4:21 Jordan Davis - **RESCUE OF THE FUNCTION OF MUTANT HERG CHANNELS USING AN INTRAGENIC POINT MUTATION**

4:21 – 4:33 Amirthagowri Ambalavanan - **IMPACT OF SLEEP DISORDERED BREATHING ON COGNITIVE BEHAVIORAL DEVELOPMENT IN CANADIAN LONGITUDINAL BIRTH COHORT**

4:35 – 4:45 Concluding Remarks and Awards

5:00 – 7:00 Reception at The Grad Club, 2nd Floor
162 Barrie Street, Kingston, ON
Cash Bar

Oral Presentations

Biomedical Engineering

FEMORAL PLAQUE QUANTIFICATION FOR THE PREDICTION OF CORONARY ARTERY DISEASE IN MEN AND WOMEN. Kayla Colledanchise, Laura-Eve Mantella, Milena Bullen, Marie-France Hétu, Joseph Abunassar, Amer M. Johri. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada. (Session 1)

Background: Cardiovascular risk remains difficult to assess in symptomatic patients, particularly in women. Femoral plaque development precedes adverse cardiovascular events, such as myocardial infarction. We sought to determine the value of a femoral plaque burden assessment, alone or combined with carotid plaque, for identifying significant angiographic coronary artery disease (CAD) in men and women. **Methods:** Five hundred participants referred for coronary angiography underwent carotid and femoral ultrasound. The extent of angiographic coronary artery luminal narrowing was established by a 4-segment model. Logistic regression was used to determine the association of carotid and femoral plaque with significant CAD ($\geq$50% stenosis) when adjusted for risk factors. Optimal cut-off values of plaque burden were determined using receiver operating characteristic curves. **Results:** In a preliminary analysis of 210 participants, femoral and carotid plaque burden independently predicted significant CAD in both men (OR range 1.01-1.61, $p<0.001$) and women (OR range 1.01-3.09, $p<0.001$). Combined femoral and carotid total plaque area was the most accurate predictor of CAD in men (cut-off $\geq$76 mm^2, 91% sensitivity, 51% specificity), while in women, CAD was most accurately predicted by a combined maximal plaque height assessment (cut-off $\geq$2.8 mm, 86% sensitivity, 53% specificity). **Conclusion:** These findings highlight the importance of utilizing sex-specific screening tools in cardiovascular risk assessment. Used clinically, vascular ultrasound may help to identify patients with significant angiographic CAD. (Supported by the Natural Sciences and Engineering Research Council of Canada, Heart and Stroke Foundation of Canada, Canada Foundation for Innovation, and the Ministry of Research, Innovation and Science).

Cancer Research and Therapy

TCF3-PBX1 ACTIVATES PROLIFERATION-PROMOTING SIGNALING PATHWAYS INDEPENDENT OF THE PRE-B-CELL RECEPTOR IN ACUTE LYMPHOBLASTIC LEUKEMIA. Jesse Leblanc[1], Changnian Shi[1], Alison M. Moore[1], Marina R. Lochhead [2], David P. LeBrun[1] , [1] Department of Pathology and Molecular Medicine, Queen's University, Kingston Ontario, Canada**,** [2] Department of Biomedical and Molecular Sciences, Queen's University, Kingston Ontario, Canada. (Session 1)

Approximately 5% of B-cell acute lymphoblastic leukemia (B-ALL) harbor a specific t(1;19) translocation which generates a fusion gene product coding for TCF3-PBX1. Recent studies have showed that t(1;19) B-ALL cases represent a distinct subset of B-ALL since they still express a functional pre-B cell receptor (pre-BCR). It is hypothesized that TCF3-PBX1 drives the leukemogenesis of these cells by promoting aberrant pre-BCR signaling through transcriptional activation of pre-BCR genes. To test this hypothesis, we've established short hairpin (shRNA) knockdown models in two different t(1;19) B-ALL cell lines (RCH-ACV and 697). When induced, these cell lines can either express a control shRNA (shControl) or a knockdown shRNA targeting the TCF3-PBX1 transcript (shPBX1). Expression of shPBX1 greatly reduced cell culture-initiation and proliferation. We then performed RNAseq in both of our knockdown models and determined that TCF3-PBX1 knockdown surprisingly activates the expression of pre-BCR components, despite a marked reduction in phosphorylation of AKT and ERK. Additionally, TCF3-PBX1 knockdown had no effect on SYK phosphorylation. Altogether, our results suggest that TCF3-PBX1 promotes t(1;19) B-ALL proliferation by activating PI3K/AKT and MAPK/ERK signaling in a pre-BCR independent manner. (Supported by the Leukemia and Lymphoma Society of Canada)

A MASS SPECTROMETRY IMAGING-BASED CLASSIFIER IDENTIFIES THE IMPORTANCE OF DYSREGULATED METABOLISM IN PROSTATE CANCER DIAGNOSIS. Nicole Morse[1], Palak Patel[1], Jenny Wang[1], Tamara Jamaspishvili[1], Kevin Ren[1], David Simon[2], Martin Kaufmann[3], Robert J. Gooding[1], David M. Berman[1], *[1] Department of Pathology and Molecular Medicine, Faculty of Health Sciences, Queen's University , [2] Department of Chemistry, Faculty of Arts and Science, Queen's University , [3] Department of Surgery, School of Medicine, Queen's University.* (Session 3)

Altered metabolism is an inherent property of cancer and provides a rich opportunity for exploring its underlying biology and developing novel diagnostic biomarkers. We used desorption electrospray ionization mass spectrometry imaging (DESI-MSI) to investigate the spatial distribution of small metabolites and lipids within prostate biopsy core tissue. We analyzed 39 prostate biopsy cores across 18 cases and selected 150x150µm regions of interest (ROIs) corresponding to cancer or benign tissue. From a training cohort of 535 ROIs across 9 cases we constructed a PCA/LDA model which achieved an AUC of 0.998 and an overall accuracy of 97%. We independently validated this model on the remaining 430 ROIs derived from 9 cases and demonstrated an overall accuracy of 85%. Hypothesis testing and log two-fold change identified 37 differentially abundant metabolites. Of these, there was increased citrate in benign tissue and increased glutamate in cancer tissue, reflective of established Krebs' Cycle alterations. We also identified increased levels of lyso-phospholipids in benign tissue and increased larger phospholipids in cancer tissue, suggesting differential biosynthesis of lipids in cancer. Ongoing studies are identifying metabolic profiles that can distinguish indolent from aggressive prostate cancer. Ultimately, the validated accuracy of this classifier, the correlation with established cancer metabolism, and the effectiveness of DESI for imaging small biopsy tissue indicates that DESI-MSI could be an effective ancillary diagnostic tool.

Cardiac, Circulatory, and Respiratory Sciences

RESCUE OF THE FUNCTION OF MUTANT HERG CHANNELS USING AN INTRAGENIC POINT MUTATION. Jordan Davis, Jun Guo and Shetuan Zhang. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada. (Session 3)

The human-ether-a-go-go-related gene (hERG) encodes the pore forming subunit of the rapidly activating delayed rectifier K^+ current (I_{Kr}) which is important for ventricular repolarization. A reduction in I_{Kr} due to loss of hERG function can lead to long QT syndrome (LQTS). Many loss-of-function hERG mutations are known to cause LQTS, the majority of which are thought to be trafficking deficient, including G601S. It has been shown that the plasma membrane (PM) expression of G601S-hERG can be rescued by reduced temperature culture. We have shown that wild-type (WT) hERG channels require extracellular K^+ for their PM stability. They undergo internalization under 0 mM K^+ culture conditions, which can be prevented by reduced temperature culture. We also identified that the S624T mutation makes hERG insensitive to extracellular K^+. We hypothesize that certain hERG mutants, including G601S, cannot sense extracellular K^+ and are unstable in the PM. In this study, we added a secondary mutation, S624T, which does not depend on extracellular K^+ for its PM expression, to the G601S mutant hERG channel. Adding S624T suppressed the loss-of-function G601S phenotype and rescued its current to near WT levels. The addition of S624T also rescued LQTS-causing hERG mutants T474I and P596R. Our data reveals the most effective intragenic rescue of LQTS-causing hERG mutants to date and lends insight into the mechanisms through which these mutations confer the loss-of-function phenotype.

SUB-HAPLOINSUFFICIENCY OF *BMPR2* CAUSES A SHIFT IN THE ENDOTHELIAL PROLIFERATIVE AND METABOLIC RESPONSE TO BMP9. Anne L. Theilmann[1], Lindsey G. Hawke[1], L. Rhiannon Hilton[1], Jodi L. Mackeil[1], Kimberly J. Dunham-Snary[1], Paula D. James[1], Donald H. Maurice[1], Stephen L. Archer[1], Mark L. Ormiston[1], [1]Queen's CardioPulmonary Unit, Queen's University, Kingston, Canada. (Session 2)

Pulmonary arterial hypertension (PAH) is a disease of occlusive vascular remodeling, which is associated with heterozygous mutations in *BMPR2*, the gene encoding the bone morphogenetic protein (BMP) type II receptor (BMPR-II) (Cogan *et al.*, 2006). Recently, the endothelial-selective BMPR-II ligand, BMP9, was shown to reverse disease in genetic and non-genetic models of PAH and suppress proliferation of healthy endothelial cells (Long *et al*, 2015). However, BMP9 has been shown to cause a shift towards excessive proliferation in cancer (Herrera *et al.*, 2009). We postulated that the development of PAH is associated with a cancer-like shift in the endothelial BMP9 response, from growth inhibition to excessive proliferation.
BMP9 treatment suppressed proliferation in control blood outgrowth endothelial cells (BOECs), surrogates for pulmonary artery endothelial cells (PAECs). PAH patient BOECs exhibited either no effect or significant proliferation in response to BMP9, which was greatest in patient BOECs exhibiting low levels of BMPR-II. siRNA knockdown of *BMPR2* in PAECs recapitulated this proliferative response to BMP9, in contrast to *siControl* treated cells, which were growth inhibited by BMP9. Assessment of metabolism, by a Seahorse analyzer showed a coupled reduction of oxidative and glycolytic metabolism in *siControl*-treated PAECs stimulated with BMP9, which was eliminated in *siBMPR2* knockdown PAECs. Our work identifies a shift in the endothelial response to BMP9 towards increased proliferation that is linked to a >50% reduction in *BMPR2*. This abstract was funded by the Canadian Institutes of Health Research and the Ontario Thoracic Society.

Health Policy, Population Health, and Epidemiology

ASSOCIATION BETWEEN HOSPITAL TEACHING STATUS AND SURVIVAL FOLLOWING TRANSJUGULAR INTRAHEPATIC PORTOSYSTEMIC SHUNT (TIPS): A POPULATION-BASED STUDY. Mah JM[1], Dewit Y[2], Menard A[3], Booth CM[1,2,4], and Flemming JA[1,2,4], Departments of [1]Medicine, [3]Radiology, and [4]Public Health Sciences, Queen's University, Kingston, ON, Canada; [2]Institute for Clinical Evaluative Sciences, Queen's University, Kingston, ON, Canada. (Session 1)

Importance: Transjugular intrahepatic portosystemic shunt (TIPS) is a procedure designed to treat portal hypertension in patients with cirrhosis. Hospital teaching status is an important institutional factor found to be predictive of outcomes following several complex procedures. Its impact on outcomes following TIPS is unknown. Objective: To determine the association between hospital teaching status and long-term survival in patients with cirrhosis receiving TIPS. Methods: Population-based, retrospective cohort study using administrative health data. Adult patients with cirrhosis who received TIPS between January 1, 1998 and December 31, 2016 were included. Hospital teaching status was defined by hospital participation in medical student instruction. Liver transplant-free (LTF) survival was evaluated using Kaplan Meier analysis and multivariate Cox regression. Results: 857 unique patients were included. 84.3% of TIPS were performed in teaching hospitals and 15.7% were performed in non-teaching hospitals. Median LTF survival was over twice as long for TIPS performed in teaching compared to non-teaching hospitals (2.2 vs. 0.9 years, P<.001). After adjusting for confounders, TIPS performed in non-teaching hospitals were associated with a 30% higher hazard of death/liver transplant compared to teaching hospitals (HR 1.30, 95% CI 1.04-1.63, P=.02). Conclusions: TIPS performed in teaching hospitals are associated with improved long-term survival. Further work is needed to understand the processes of care that contribute to improved outcomes in teaching hospitals and to determine whether centralization of TIPS is warranted.

Inflammation, Infection and Immunity

INTERLEUKIN-27 DIFFERENTIALLY MODULATES TOLL-LIKE RECEPTOR 7 AND 8 FUNCTION IN HUMAN MONOCYTES AND MACROPHAGES. Natalya Odoardi[1], Carlene Petes[1], Katrina Gee[1,] [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada. (Session 2)

Interleukin (IL)-27 is a heterodimeric cytokine composed of two subunits which has been shown to have modulatory effects on the Toll-like receptors (TLRs) of cells from myeloid origin. TLRs are important innate immune sensors that provide the first line of defense against invading pathogens. Specifically, TLR7 and TLR8 are found within the endosome of various immune cells, such as monocytes and macrophages, and recognize single-stranded RNA or synthetic RNA analogs. Upon recognition of their corresponding ligand, a MyD88-dependent signalling cascade is initiated resulting in the nuclear translocation of NF-κB, among other transcription factors, and pro-inflammatory cytokine and type I interferon production. The efficiency of an immune response is governed by the production of cytokines. Focusing on examining the effects of IL-27 on endosomal TLR7 and TLR8, we analyzed expression and cytokine production to determine how IL-27 modulates innate immune responses. Analysis of IL-27 treated monocytes and macrophages revealed changes in mRNA and protein expression of TLR7 and TLR8. Treatment with IL-27 also enhanced TLR function by increasing pro-inflammatory cytokine secretion. This investigation suggests that IL-27 has modulatory effects on endosomal TLRs which enhances signaling and pro-inflammatory cytokine production. Delineating the immunomodulatory role of IL-27 on TLR7 and TLR8 responses will provide insight into how its mechanistic actions can be applied to improve viral vaccine development and novel adjuvant research and design. Research supported by Natural Sciences and Engineering Research Council (NSERC). NO is supported by CGS-M.

Neuroscience Research

CEREBROSPINAL FLUID BIOMARKERS IN A NONHUMAN PRIMATE MODEL OF ALZHEIMER'S DISEASE. Emma Robertson[1], Susan Boehnke[1], Fernanda De Felice[1,2], Douglas Munoz[1]. Centre for [1]Neuroscience Studies, Queen's University, [2]Federal University of Rio de Janeiro, Brazil. (Session 3)

Alzheimer's disease (AD) pathology, such as amyloid plaques and neurofibrillary tangles, can be observed in humans before the onset of behavioural symptoms (Sperling et al., 2011). These pathological changes can be analyzed in cerebrospinal fluid (CSF). Changes in CSF levels of amyloid-β 1-40 (Aβ40), amyloid-β 1-42 (Aβ42), total tau proteins (tTau), phosphorylated tau Thr181 (pTau), and neurofilament light (NFL) have been implicated as biomarkers of human AD. Here we sought to determine if these CSF biomarkers also change in a recently developed nonhuman primate (NHP) model of AD (Forny-Germano et al., 2014). CSF samples were collected through lumbar punctures in control NHPs to establish baseline biomarker values. First, lumbar puncture procedures were optimized. We found that needle insertion into the vertebral space of cynomolgus macaques at 2.9 cm yielded successful CSF sample collection, while for rhesus macaques it was 3.1 cm. In these control NHPs, baseline values of Aβ40, Aβ42, tTau, pTau and NFL showed variability, but were similar between species. Importantly, we also found that these AD biomarkers tend to be elevated in NHPs receiving injections of amyloid beta oligomers and not in a control animal receiving injections of vehicle. Thus, these changes in CSF may be reflective of developing AD-related pathology in the brain and will allow us to investigate disease progression, pathological mechanisms and novel therapeutics in NHPs. (Supported by CIHR and Brain Canada)

Patient Care and Nursing

CULTURAL HUMILITY AND TRANSGENDER CLIENTS: A STUDY EXAMINING THE RELATIONSHIP BETWEEN CRITICAL REFLECTION AND ATTITUDES OF NURSE PRACTITIONERS. Jennifer Carroll, BScN, RN, Master of Nursing Science Student, Queen's University Rosemary Wilson, RN(EC), PhD, Associate Professor, School of Nursing, Queen's University Elizabeth G. VanDenKerkhof RN DrPH, Professor and Sally Smith Chair in Nursing, School of Nursing, Queen's University, Dana S. Edge PhD, RN, Associate Professor, School of Nursing, Queen's University. (Session 1)

Transgender people are increasingly being treated by primary care providers, including Nurse Practitioners (NPs), for care surrounding social, legal, medical, or surgical transition. The purpose of this study was to develop an understanding of Ontario NPs' care of transgender clients. The primary research question explored the relationship between critical self-reflection, a key attribute of cultural humility, and attitudes towards transgender clients. Cultural humility is a recent and important progression from the cultural competency approach to caring for diverse client populations. Within the cultural humility perspective, an expanded definition of diversity is acknowledged, and the foundational attribute of critical self reflection is emphasized. This oral presentation provides preliminary results of a 2017 descriptive, cross-sectional survey of Ontario Nurse Practitioners practicing in primary care. Attendees will be invited to participate in discussion of the findings. Participants will have a better understanding of policy and practice changes in trans care and the need for culturally humble care. Key constructs measured: critical reflection, attitudes, experience, awareness.

Protein Structure and Function

DEFINING THE MOLECULAR BASIS OF MICROTUBULE LENGTH REGULATION IN CANDIDA ALBICANS. Byron Hunter, Irsa Shoukat, Dasha Trofimova, Corey Frazer, and John Allingham. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada. (Session 2)

An important signature of pathogenesis development in *Candida albicans* is the transition from a budding yeast state into hyphae. Achieving this morphological switch is, in part, dependent upon rapid reorganization of the microtubule cytoskeleton network by microtubule regulatory factors that catalyze addition or removal of tubulin dimers from microtubule ends. Molecular motors of the kinesin-8 family have been shown to play a major role in regulating microtubule dynamics within dividing cells, but their role(s) in the yeast-to-hyphal transition and in highly polarized cells are unknown. Our lab has shown that *C. albicans* cells lacking the kinesin-8 motor Kip3 are unable to form hyphae. Moreover, budding *kip3*-null cells have abnormally thick anaphase spindles, and cytoplasmic microtubules that are exceptionally long and persistent. These findings indicate that Kip3 may act as a microtubule depolymerase, and suggest that microtubule length control is vital to the yeast-to-hyphal transition. To confirm its microtubule depolymerase activity, we show that purified Kip3 constructs can shorten microtubules in a catalytic manner *in vitro*, and that this activity is contained within the motor domain region of the enzyme. We also elucidated an X-ray crystal structure of the Kip3 motor domain and determined the physical shape and stoichiometry of Kip3-tubulin complexes by small angle x-ray scattering, shedding light on its depolymerization mechanism.(Supported by the Natural Sciences and Engineering Research Council of Canada).

MOLECULAR CO-EVOLUTION OF COAGULATION FACTOR VIII AND VON WILLEBRAND FACTOR. Philip M. Zakas, Christopher W. Coyle, Caelan Radford, Christine Brown, Kate Nesbitt, Courtney Dwyer, Eric Gaucher, Christopher B. Doering, David Lillicrap**,** Department of Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, Canada. (Session 2)

Von Willebrand disease (VWD) and hemophilia A (HA) are the most prevalent inherited bleeding disorders in the global population. These disorders arise from qualitative or quantitative deficiencies in either von Willebrand factor (VWF) or coagulation factor VIII (FVIII), respectively. Each protein is the product of distinct genes on different chromosomes, however, their role in hemostasis is coordinated and concomitant. These proteins circulate in a non-covalent complex, protecting FVIII from proteolytic degradation and clearance. It remains unclear how the dependence of FVIII on VWF emerged, however, it has persisted in every species investigated. It has been widely observed that species-specific differences in FVIII biosynthesis, biochemistry, and immunology exist. While species-specific differences in VWF biology have also been observed regarding platelet activation, there has been limited investigation into the FVIII-VWF interaction across species. In this study, we characterize the molecular evolution of mammalian VWF using ancestral sequence reconstruction (ASR) and investigate the co-evolution of FVIII and VWF. We produced and characterized 5 ancestral VWF sequences spanning several mammalian lineages. Our data demonstrate that ancestral VWF retained conserved intracellular and extracellular structure but displayed variable biosynthetic efficiencies, activities, and clearance rates. Although VWF and FVIII changed dramatically across mammalian clades, each protein changed in coordination with the other. This report provides the first phylogenetic and biochemical evidence of molecular coevolution within the hemostatic system.(Supported by Canadian Institutes of Health Research)

Reproductive and Sexual Function

INTERVENING IN THE POSTNATAL PERIOD IN A MOUSE MODEL OF PREECLAMPSIA-INDUCED OFFSPRING COGNITIVE AND NEUROANATOMICAL ALTERATIONS. Vanessa R. Kay[1], Lindsay Cahill[2], Anas Hanif[1], Chandrakant Tayade[1], John G. Sled[2], B. Anne Croy[1]**,** [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada**,** [2]MICe, Hospital for Sick Children, Toronto, ON, Canada. (Session 2)

Background: Offspring of preeclamptic pregnancies have life-long cognitive alterations. *In utero* treatment is complicated by the placental barrier. The neonatal period may be a window for intervention. Placental growth factor (PGF) is deficient in preeclampsia and *Pgf*$^{-/-}$ mice model the offspring effects of a preeclamptic-gestation. We investigated if postnatal PGF treatment corrects adult behaviour, neuroanatomy and cerebrovascular deficits in *Pgf*$^{-/-}$ mice. **Methods:** C57BL/6-*Pgf*$^{-/-}$ pups were weighed and treated postnatal day (P)1-10 with phosphate-buffered saline (PBS) or PGF at doses of 10pg/g (physiological), 70pg/g (peak gestational) or 700pg/g (supraphysiological) i.p. As adults, mice underwent the Open Field Test (OFT), Tail Suspension Test (TST) and Y-maze Spontaneous Alternation Test (YMSAT). Mice were perfused for magnetic resonance imaging (MRI) of neuroanatomy or for micro-computed tomography (μCT) imaging of cerebrovasculature. **Results:** Pup weights were less in the treated groups beginning P7 but adult weights did not differ. On the OFT, 10 pg/g-treated mice exhibited decreased time moving ($p<0.0001$), total distance travelled ($p=0.0033$) and percent of time spent in the centre ($p=0.0003$). In the TST, time to immobility showed a sex-specific, dose-dependent increase and was higher in 700 pg/g-treated females ($p<0.0001$). There was no difference in YMSAT performance. MRI and μCT image analyses are continuing. **Conclusion:** PGF replacement altered behaviour in *Pgf*$^{-/-}$ mice suggesting the postnatal period is a window to correct developmentally-induced deficits. **Funding sources:** *NSERC, CIHR*

IMPACT OF SLEEP DISORDERED BREATHING ON COGNITIVE BEHAVIORAL DEVELOPMENT IN CANADIAN LONGITUDINAL BIRTH COHORT. Amirthagowri Ambalavanan[1], Jihoon Choi[1], Amel Lamri[3], Sukhpreet K. Tamana[4], Sonia Anand[4], Diana Lefebvre[3], Malcolm Sears[4,6], Padmaja Subbarao[5,6,7], Piush Mandane[4], Qingling Duan[1,2], [1] Department of Biomedical and Molecular Sciences, Queen's University, [2] School of Computing, Queen's University, [3] Department of Clinical Epidemiology and Biostatistics, McMaster University, [4] Department of Pediatrics, University of Alberta, [5] The Hospital for Sick Children, [6] Department of Medicine, McMaster University, [7] Department of Paediatrics, University of Toronto. (Session 3)

Sleep disordered breathing (SDB) is a collective term for chronic conditions include habitual snoring and obstructive sleep apnea. SDB is highly prevalent among the children as it affects up to 10% of them between 2 and 8 years of age resulting poor quality of life and cognitive ability. Little is known about the disease causality of SDB in children. In our current study, we ascertained the genomics data (Illumina HumanCore Exome BeadChip) from the largest birth cohort (N=3455) in Canada known as the Canadian Healthy Infant Longitudinal Development (CHILD) study. The Edmonton site of the CHILD cohort constituting about 700 subjects were diagnosed for the longitudinal impact of preschool SDB (between 3 months and 5 years) and their clinical outcomes such as executive functioning and externalizing behaviour. We will perform a multivariate SNP collapsing method to test the association of selective genes with various child behaviour checklist scores. Studies have shown that early life exposures are major factors in the development of chronic respiratory conditions and sleep disorders. Hence, we will further investigate the gene and environmental associations based on information (parental SDB, sleep duration, apnea-hypopnea index, sleep habits, and physical activity) obtained from parent reported questionnaires. We speculate that this approach will lead to the identification of candidate genes potentially involved in sleep disorders, and their impact on cognitive development in children.

Poster Presentations

Biomedical Engineering

1. **DEVELOPMENT OF A VASCULARIZED CAROTID ARTERY PLAQUE PHANTOM FOR THE INVESTIGATION OF NOVEL ULTRASOUND-BASED THERAPIES.** Christie Boswell-Patterson[1], Olivia Yau[2], MSc, Stephen Pang[1], PhD, Man Yat Tse[1], PhD, Jianhua Zhou[3], PhD, Marie-France Hétu[2], PhD, Amer M. Johri[1,2], MD, MSc, FRCPC, FASE. [1] Department of Biomedical and Molecular Sciences, Queen's University. [2] Department of Medicine, Queen's University. [3] School of Engineering, Sun Yat-Sen University, Guangzhou, China.

2. **DETECTING LOW BACK PAIN FROM CLINICAL NARRATIVES USING MACHINE LEARNING APPROACHES.** Michael Judd[1], Farhana Zulkernine[1], Brent Wolfrom[2], Akshay Rajaram[2], David Barber[2]. [1] School of Computing, Queen's University, Kingston, Ontario [2] Department of Family Medicine, Queen's University, Kingston, Ontario.

3. **DEVELOPING A SIMULATION CURRICULUM TO TEACH MEDICAL STUDENTS TO PERFORM AN ULTRASOUND-GUIDED NEEDLE INSERTION.** Sachin V. Pasricha[1,2], Zsuzsanna Keri[1], Matthew S. Holden[1], and Gabor Fichtinger[1]. [1]Laboratory for Percutaneous Surgery, School of Computing, Queen's University, Kingston, ON, Canada [2]School of Medicine, Queen's University, Kingston, ON, Canada.

4. **COMPARISON OF 3D ULTRASOUND IMAGING TO COMPUTED TOMOGRAPHY IN KNEE OSTEOPHYTE DEPICTION.** Vendries, V (MSc, BSc), Ungi, T (PhD, MD), Harry, J, Kunz, M (PhD), MacKenzie, L (PhD), Venne, G (PhD, D.O) Department of Biomedical and Molecular Sciences, Queens University.

5. **AN EDGE COMPUTING FRAMEWORK TO RECEIVE AND PROCESS STREAMING WEARABLE SENSOR DATA FOR PATIENT MONITORING** Dharmitha Ajerla. Sazia Mahfuz, Farhana Zulkernine, School of Computing.

Cancer Research and Therapy

6. **CLASSIFYING PATHWAYS TO THE DIAGNOSIS OF COLORECTAL CANCER: A NEW APPROACH USING ADMINISTRATIVE DATA IN ONTARIO.** Zhen Guan1,2, Colleen Webber2, Jennifer Flemming2, Bingshu Chen3, Patti Groome1,2 Department of Public Health Sciences, Queen's University, Kingston, ON, Canada Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute, Queen's University, Kingston, ON, Canada Canadian Cancer Trials Group, Queen's University, Kingston, ON, Canada

7. **THE IMPACT OF NAT1 GENETIC POLYMORPHISM ON CATALYTIC ACTIVITY IN THE HUMAN COLON MUCOSA**. Griffin Pauli, Sandra Graham, Dr. Thomas Massey, Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

8. **THE ROLE OF FUCOSYLATION ON SPHEROID FORMATION FROM CHEMORESISTANT PROSTATE CANCER CELLS**. Regina-Veronicka Kalaydina, Hedi Zhou and Myron R Szewczuk. Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

9. **INTERLEUKIN-27: A POTENTIAL CYTOKINE TO COMBAT AGGRESSIVE METASTATIC PROSTATE CANCER?** Olena Kourko[1], Daniela Cino[1], Robin Smyth[1], Carlene Petes[1], Kyle Seaver[1], Natalya Odoardi[1], Sameh Basta[1], Katrina Gee[1] [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

10. **ROLE OF THE PROGRAMMED DEATH LIGAND 1 (PD-L1) IMMUNE CHECKPOINT IN THE ACQUISITION OF MALIGNANT PHENOTYPES IN TUMOUR CELLS** Minassian L[1,2], Sanwalka D[1,2], Macdonald-Goodfellow S[1,2], Ghaffari A[1,2], Craig A, Siemens[1,2,3] DR, Graham CH[1,2,3] *1) Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada. 2) Cancer Research Institute, Queen's University, Kingston, Ontario, Canada. 3) Department of Urology, Kingston General Hospital, Kingston, Ontario, Canada.*

11. **IDENTIFYING BIOMARKERS OF RESPONSE TO WEE1 INHIBITOR (AZD1775) AND ITS EFFECT ON THE TUMOUR IMMUNE MICROENVIRONMENT IN HIGH-GRADE SEROUS OVARIAN CANCER.** Sarah Nersesian, Nichole Peterson, Julie Ann-Francis, Carlos Escobedo and Madhuri Koti.

12. **AUTOPHAGY IS REQUIRED FOR TUMOUR CELL DRUG RESISTANCE INDUCED BY THE PROGRAMMED DEATH LIGAND 1 (PD-L1) IMMUNE CHECKPOINT.** Sanwalka, D.[1], Minassian L.M.[1], Sutherland, L.[1], MacDonald-Goodfellow S.[1], Ghaffari, A.[1], Koti, M.[1], Siemens, D.R.[1,2] and Graham, C.H.[1,2] 1. Department of Biomedical and Molecular Sciences, Queen's University 2. Department of Urology, Kingston General Hospital.

13. **EVALUATING THE EFFICACY AND IMMUNOGENICITY OF A PROPHYLACTIC CANCER VACCINE.** Kyle Seaver[1], Peter Greer[2] and Sam Basta[1]. [1]Department of Biomedical & Molecular Science Queen's University, Kingston, Ontario, Canada. [2]Division of Cancer Biology and Genetics, Cancer Research Institute, Department of Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, Canada.

14. **REGIONS CONNECTING THE MEMBRANE SPANNING AND NUCLEOTIDE BINDING DOMAINS OF MULTIDRUG RESISTANCE PROTEIN 1 (MRP1) ARE FUNCTIONALLY DISTINCT**. Emma E. Smith, Gwenaëlle Conseil and Susan P. C. Cole,Department of Pathology and Molecular Medicine.

15. **A PHARMACOGENOMICS ANALYSIS OF BIOLOGICAL NETWORKS REGULATING CHEMOTHERAPY RESPONSE AMONG OVARIAN CANCER PATIENTS.** Danai G. Topouza[1], Jihoon Choi[1], Sean Nesdoly[2] and Qingling Duan[1,2]. [1]Department of Biomedical and Molecular Sciences, Queen's University [2]Queen's School of Computing, Queen's University Kingston, Ontario, Canada.

16. **STAT1 EXPRESSION ASSOCIATES WITH PD-L1 AND IDO1 IMMUNE CHECKPOINT GENE EXPRESSION IN HIGH-GRADE SEROUS OVARIAN CANCER.** Thiago Vidotto, Nichole Peterson, Barbara Vanderhyden, Manon de Ladurantaye, Anne-Marie Mes-Masson, Julie-Ann Francis, Madhuri Koti. Department of Biomedical and Molecular Sciences, Queen's University.

17. **LOSS OF PTEN DECREASES THE PROSTATE CANCER CELL-INTRINSIC TYPE I INTERFERON RESPONSE.** Natasha Vitkin1, Nichole Peterson2, D. Robert Siemens3, Madhuri Koti1,2,4 1) Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada. 2) Division of Cancer Biology and Genetics, Queen's University, Kingston, Ontario, Canada. 3) Department of Urology, Queen's University, Kingston, Ontario, Canada. 4) Department of Obstetrics and Gynecology, Queen's University, Kingston, Ontario, Canada.

18. **MICRORNA-BASED CLASSIFICATION OF GASTROINTESTINAL NEUROENDOCRINE TUMORS**. Justin Wong[1], Nicole Panarelli[2], Kathrin Tyryshkin[1], Adrianna Majewski[1], Xiaojing Yang[1], Theresa Scognomaglio[2], Michelle Kim[3], Kimberley Bogardus[4], Thomas Tuschl[4], Yao-Tseng Chen[2], Neil Renwick[1,4]. [1]Laboratory of Translational RNA Biology, Queen's University, Kingston, ON, Canada; [2]Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY, USA; [3]Center for Carcinoid and Neuroendocrine Tumors of Mount Sinai, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]HHMI_Labratory of RNA Molecular BIology, The Rockefeller University, New York, NY, USA.

19. **REGULATION OF DIFFERENTIATION OF BALB/C3T3-DERIVED PREADIPOCYTES BY CRAC1.** Veronica Youssef, Stephanie Guy, Yichang Huang, Evangelia Tomai, Leda Raptis

20. **DIFFERENTIAL PHOSPHORYLATION OF THE SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION-3 (STAT3) AND THE DOMINANT-NEGATIVE MUTANT STAT3β, FOLLOWING CADHERIN ENGAGEMENT *VS* EXPRESSION OF ACTIVATED SRC^{527F}.** Veronica Youssef, Zaid Taha, Mulu Geletu, Leda Raptis

Cardiac, Circulatory, and Respiratory Sciences

21. **THE IMPACT OF ISOMETRIC HANDGRIP TRAINING (IHGT) ON CARDIOVASCULAR REACTIVITY TO ACUTE MENTAL STRESS**. Kaitlyn R. Liu, Sarah E. Bailey, Morgan D. Silvester, Kyra E. Pyke, Queen's University, Kingston, Ontario, Canada, School of Kinesiology and Health Studies (Cardiovascular Stress Response Lab)

22. **MECHANICAL STRETCH STIMULATES THE ACTIVITY OF POTASSIUM CHANNEL KV1.5.** Alexandria Milton, Wentao Li, Jun Guo, Shawn Lamothe, and Shetuan Zhang, Department of Biomedical and Molecular Sciences, Queen's University.

23. **DEVELOPMENT OF A CARDIAC ULTRASOUND LEARNING MODULE TO ENHANCE THE TEACHING OF ANATOMY IN MEDICAL SCHOOLS**. Salwa Nihal, Joshua N. Durbin, Terry Li, Abbas Rizvi, Stephen C. Pang and A.M. Johri. Department of Biomedical & Molecular Sciences and Division of Cardiology, Department of Medicine, Queen's University.

24. **NATURAL KILLER CELL HOMEOSTASIS, INTERLEUKIN-15 AND TRANSFORMING GROWTH FACTOR-B SIGNALING IN THE CHRONIC HYPOXIA MOUSE MODEL OF PULMONARY ARTERIAL HYPERTENSION.** Matthew T. Rätsep[1], Rhiannon Hilton[2], Melissa Mitchell[2], Maureen O'Connor-McCourt[3], and Mark L. Ormiston[1,2], Departments of Medicine[1] and Biomedical and Molecular Sciences[2], Queen's University, Kingston, Ontario, Canada and Formation Biologics Inc.[3], Montreal, Quebec, Canada.

25. **DIFFERENTIAL REGULATION OF HERG CURRENT AND EXPRESSION BY ACTIVATION OF PROTEIN KINASE C.** Morgan Sutherland-Deveen, Jun Guo, Wentao Li, Jihang Yu, Shawn M. Lamothe, and Shetuan Zhang, Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

26. **MOLECULAR MECHANISMS OF FENTANYL-MEDIATED SUDDEN DEATH.** Jared Tschirhart, Wentao Li, Jun Guo, Shawn Lamothe, and Shetuan Zhang**,** Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

27. **ACUTE HYPERGLYCEMIA IMPAIRS ARTERY FUNCTION DURING THE LOW ESTROGEN, BUT NOT THE HIGH ESTROGEN, PHASE OF THE MENSTRUAL CYCLE.** JS Williams, T Stimpson, JC Tremblay, AM Fenuta, KE Pyke, School of Kinesiology and Health Studies, Queen's University, Kingston, Ontario.

Health Policy, Population Health, and Epidemiology

28. **THE RELATIONSHIP BETWEEN ESTABLISHED RISK FACTORS FOR COLORECTAL CANCER AND LINE-1 DNA METHYLATION**. Gogna P[1], King WD[1], [1]Department of Public Health Sciences, Queen's University.

29. **SCHOOL-BASED RELATIVE AGE EFFECTS IN CANADIAN ADOLESCENTS: A MENTAL HEALTH FOCUS.** Nathan King, MSc, Colleen Davison, PhD, William Pickett, PhD, Department of Public Health Sciences, Queen's University Kingston, Ontario Canada.

30. **PSYCHOMETRIC ANALYSIS OF TWO NEW SCALES TO ASSESS TEACHERS' CONFIDENCE IN DELIVERING MENTAL HEALTH RELATED CONTENT IN THE CLASSROOM.** Brooke Linden, Dr. Heather Stuart**,** Public Health Sciences.

31. **A RANDOMIZED-CONTROL TRIAL OF MULTI-PLATFORM AUDIOVISUAL TEACHING MODULES IN COLORECTAL SURGERY LEARNING PRESERVATION.** *Candy S, Mir ZM, Hanna N, Zevin B, & Patel SV.* Department of Surgery.

32. **EMOTIONAL AND PHYSICAL CHILD ABUSE IN THE CONTEXT OF THE 2010 HAITI EARTHQUAKE.** Sony Subedi , Colleen Davison and Susan Bartels, Department of Public Health Sciences.

33. **A POPULATION BASED COHORT STUDY ON THE TRENDS OF CHILDHOOD INTUSSUSCEPTION IN ONTARIO.** Arany Theivendram[1], Mila Kolar[2], Michael McIsaac[1] and Susan Brogly[2]. [1]Department of Public Health Sciences and [2]Department of Surgery, Queen's University, Kingston, Ontario, Canada.

Inflammation, Infection and Immunity

34. **EVALUATING CYTOKINE PRODUCTION BY DIFFERENT MACROPHAGE SUBSETS IN RESPONSE TO VIRUS INFECTION.** Torki Alothaimeen[1], Sam Basta[1] and Katrina Gee[1]. [1]Department of Biomedical & Molecular Science Queen's University, Kingston, Ontario, Canada.

35. **TEMPORAL ANALYSIS OF CHRONIC SPINAL CORD INJURY PAIN.** Courtney Bannerman[1], Julia Segal[1], Jaqueline Silva[1], Scott Duggan[2], Nader Ghasemlou[1,2] [1]Department of Biomedical and Molecular Sciences, [2]Department of Anesthesiology.

36. **THE MICROBIOME: A NOVEL MODULATOR OF THE FVIII IMMUNE RESPONSE.** Tarrant J, Cormier M, Nesbitt K, Dwyer C, Hough C, and David Lillicrap. Department of Pathology and Molecular Medicine, Queen's University Kingston, Ontario Canada.

37. **IL-27 AMPLIFIES CYTOKINE RESPONSES TO GRAM-NEGATIVE BACTERIAL PRODUCTS AND SALMONELLA TYPHIMURIUM INFECTION**. Carlene Petes1, Natalya Odoardi1, Samantha M. Plater1, Nancy L. Martin1, Katrina Gee1,1 Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

38. **INVESTIGATING THE SIGNALING PATHWAYS OF MURINE MACROPHAGES AFTER STIMULATION OF TLR-7 WITH SSRNA ANALOGUES AND VIRUS INFECTION.** Evan Trus[1], Torki Alothaimeen[1], Katrina Gee[1], Sam Basta[1], [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

Neuroscience Research

39. **CHARACTERIZING RESPONSE INHIBITION DEFICITS IN ADOLESCENTS SHOWING EARLY SIGNS OF BORDERLINE PERSONALITY DISORDER USING AN OCULOMOTOR TASK.** O. G. CALANCIE[1], A. C. PARR[1], L. BOOIJ[2], D. BRIEN[1], B. C. COE[1], S. KHALID-KHAN[1], D. P. MUNOZ[1], [1]Centre for Neuroscience Studies, [2]Psychology, Queen's Univ., Kingston, ON, Canada.

40. **MEMORY LABILITY, RETRIEVAL PRACTICE & LONG-TERM MEMORY IN A HUMAN GROSS ANATOMY COURSE**. Joshua C. Goheen, Ronald A. Easteal, Mohammad B. Azzam, Rylan G. Egan and Carolyn J. Perry. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON K7L 3N6, Canada.

41. **IDENTIFICATION OF CO-EXPRESSION NETWORK ASSOCIATED WITH CHRONIC PAIN IN SPINAL CORD INJURY PATIENTS.** Suleman Gul Khan[1], Margot Gunning[1], Jihoon Choi[1], Courtney Bannerman[1], Nader Ghasemlou[1], Qingling Duan[1,2], [1] Department of Biomedical and Molecular Sciences, Queen's University, [2] School of Computing, Queen's University.

42. **POPULATION DYNAMICS IN A RODENT MODEL OF FOCAL ISCHEMIC STROKE: BARRIER TO PRE-CLINICAL THERAPEUTIC TRANSLATION?** Kathleen A. Harrison & Douglas J. Cook. Centre for Neuroscience Studies, Queen's University Kingston, Ontario Canada.

43. **MORPHOMETRIC ANALYSIS OF DORSAL HIPPOCAMPAL NEURONS IN A MOUSE MODEL OF SPORADIC ALZHEIMER'S DISEASE**. Rasha H. Mehder, Brian M. Bennett, R David Andrew, Department and Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

44. **RETRIEVAL PRACTICE FOR LEARNING LEADING TO BETTER LONG-TERM RETENTION AND IMPROVED STUDENT PERFORMANCE**. Mohammad B. Azzam, Ronald A. Easteal, Joshua C. Goheen, and Rylan G. Egan. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON K7L 3N6, Canada.

45. **AROMATASE EXPRESSION IN THE NEOCORTEX OF ADULT MALE RATS.** Chloe N. Soutar[1] , Patrick Grenier[2] , Mary C. Olmstead[1, 2], and Hans C. Dringenberg[1, 2] , [1]Centre for Neuroscience Studies, Queen's University, Kingston, ON, [2]Department of Psychology, Queen's University, Kingston, ON.

46. **INDUCED CELL-MEDIATED DELIVERY OF GLIAL CELL LINE DERIVED NEUROTROPHIC FACTOR IS NEUROPROTECTIVE FOR MYENTERIC NEURONS**. Demetri P. Zoumboulakis, Sandra Lourenssen, Jacob Pyche, Michael Blennerhassett, Department of Medicine, GIDRU, KGH.

Patient Care and Nursing Research

47. **SPEAC (SAMPLING PATIENT EXPERIENCE TO ASSESS COMMUNICATION): A PILOT IMPLEMENTATION STUDY IN CLINICAL CLERKSHIP.** Sachin Pasricha[1], Juliana Sunavsky[1], Adam Mosa[1], MSc, Eleni Katsoulas[2], MEd, Andrea Winthrop[2,3], MD, FRCS(C), [1]School of Medicine, Queen's University, [2]Undergraduate Medical Education Program, Queen's University, [3]Department of Surgery, Queen's University

48. **CONCEPT ANALYSIS OF BODILY INTEGRITY IN INFANTS BORN INTERSEX/WITH DISORDERS OF SEX DEVELOPMENT.** Jennifer Carroll, BScN, RN, Master of Nursing Science Student, Queen's University, Rosemary Wilson, RN(EC), PhD, Associate Professor, School of Nursing, Queen's University.

Protein Structure and Function

49. **REGIONS CONNECTING THE MEMBRANE SPANNING AND NUCLEOTIDE BINDING DOMAINS OF MULTIDRUG RESISTANCE PROTEIN 1 (MRP1) ARE FUNCTIONALLY DISTINCT.** Emma E. Smith, Gwenaëlle Conseil and Susan P. C. Cole, Department of Pathology and Molecular Medicine.

50. **PERCEIVED DISTANCE TO SPECIALIST MEDICAL CARE AND OBSTRUCTIVE SLEEP APNEA DIAGNOSIS IN RURAL SASKATCHEWAN.** Catherine Spagnuolo[1], Michael McIsaac[1], James Dosman[2], Chandima Karunanayake[2], Punam Pahwa[2] and William Pickett[1], [1]Department of Public Health Sciences, Queen's University, [2]Canadian Centre for Health and Safety in Agriculture, University of Saskatchewan

51. **THE ROLE OF THE *FUSARIUM GRAMINEARUM* STE2P RECEPTOR IN THE PATHOGENIC INFECTION OF WHEAT.** Pooja Sridhar[1], Daria Trofimova[1], John Allingham[1], Michele Loewen[1,2], [1]Queen's University, Department of Biomedical and Molecular Sciences, Kingston, Canada.[2]National Research Council of Canada, Ottawa, Canada.

52. **ENGINEERING A MULTI-FUNCTIONAL CAZYME COMPLEX WITH ENHANCED AGAROSE-DEGRADING PROPERTIES.** Keegan B. Turner-Wood, Julie Grondin, Benjamin Pluvinage, Alisdair B. Boraston, Holly L. Spencer, Steve Smith**,** Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada. (Supported by NSERC)

Rehabilitation Science

53. **HEALTH SCIENCES RESEARCH USING ONLINE METHODS: CONSIDERATIONS FOR NOVICE RESEARCHERS.** Shikha Gupta and Atul Jaiswal, PhD Candidates, School of Rehabilitation Therapy, Queen's University.

Reproductive and Sexual Function

54. **EFFECTS OF CARBON MONOXIDE ON VASCULAR ADAPTATIONS DURING PREGNANCY.** Megan Dickson[1], Karalyn McRae[1], Nichole Peterson[1], Graeme Smith[1,2]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, [2]Department of Obstetrics and Gynaecology, Queen's University, Kingston, Ontario.

55. **THE NOVEL POST-ACTIVATION INVOLVEMENT OF POST-ACROSOMAL SHEATH RESIDENT GLUTATHIONE-S-TRANSFERASE OMEGA 2(GSTO2) IN NUCLEAR DECONDENSATION AND MALE PRONUCLEAR FORMATION.** Hamilton, Lauren E.[1], Suzuki, Joao[2], Mao, Jiude[3], Mienhson, Marie Charlotte[2], Xu, Wei[1], Sutovsky, Peter[3,4], and Richard Oko[1]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada**,** [2]Department of Veterinary Sciences, Center for Research in Reproduction and Fertility, Universite de Montreal, St. Hyacinthe, QC, Canada**,** [3]Division of Animal Sciences, College of Food, Agriculture and Natural Resources, and [4]Department of Obstetrics, Gynecology and Women's Health, School of Medicine, University of Missouri, Columbia, Missouri, USA.

56. **NON-NUCLEAR CORE SOMATIC HISTONES ARE NOVEL CONSTITUENTS OF THE RAT PT AND APPEAR TO BE *DE NOVO* SYNTHESIZED DURING SPERMIOGENESIS.** Morgan Lion[1], Genevieve Acteau[1], Lauren Hamilton[1], Nicole Protopapas[1], Wei Xu[1], Peter Sutovsky[2,3], and Richard Oko[1], [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, [2]Division of Animal Sciences, College of Food, Agriculture and Natural Resources, and [3]Department of Obstetrics, Gynecology and Women's Health, School of Medicine, University of Missouri, Columbia, Missouri, USA.

57. **IL-13 AND IL-33 POLARIZE MACROPHAGES TO THE M2 PHENOTYPE AND CONTRIBUTE TO ENDOMETRIOSIS PATHOPHYSIOLOGY.** Ryan M. Marks[1], Jessica M. Miller[1], Vanessa R. Kay[1], Lindsey K. Symons[1], Asgerally T. Fazlebas[2], Chandra Tayade[1,] [1]Department of Biomedical and Molecular Science, Queen's University, Kingston, ON Canada, [2]Obstetrics, Gynaecology and Reproductive Biology, Michigan State University, Lansing, MI USA.

58. **THE POST-ACROSOMAL SHEATH AND PERFORATORIAL REGIONS OF THE PERINUCLEAR THECA OF RAT SPERMATOZOA SHARE COMMON DEVELOPMENTAL ORIGINS AND PROTEIN CONSTITUENTS**. Nicole Protopapas[1], Lauren Hamilton[1], Wei Xu[1], Peter Sutovsky[2,3], and Richard Oko[1]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, [2]Division of Animal Sciences, College of Food, Agriculture and Natural Resources, and [3]Department of Obstetrics, Gynecology and Women's Health, School of Medicine, University of Missouri, Columbia, Missouri, USA.

Therapeutics and Toxicology

59. **MECHANISMS OF CEREBRAL VASCULAR PATHOLOGY IN A NEW ANIMAL MODEL OF AGE-RELATED COGNITIVE IMPAIRMENT.** Ahmed M. Elharram, Rebecca D. Maciver, Mandy E. Turner, Michael A. Adams and Brian M. Bennett. Department of Biomedical and Molecular Sciences and Centre for Neuroscience Studies, Queen's University, Kingston Ontario Canada.

60. **HIGH DOSE CALCITRIOL INDUCES VASCULAR CALCIFICATION IN NON-CKD RATS**. Corey M. Forster1, Mandy E. Turner1, Kimberly J. Laverty1, Emilie C. Ward1, Cynthia M. Pruss1, Rachel M. Holden2, Michael A. Adams1, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON, Canada, 2Department of Medicine, Queen's University, Kingston ON, Canada.

61. **INVESTIGATING PERTURBATIONS OF CD1 MOUSE FETAL TOPOISOMERASE IIA FOLLOWING BENZOQUINONE EXPOSURE.** Trent H. Holmes and Louise M. Winn. Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

62. **ACUTE RESPONSE TO VITAMIN D TREATMENT IS ATTENUATED IN PROGRESSING EXPERIMENTAL CKD.** Lok Hang Lee[1], Mandy E. Turner[1], Emilie Ward[1], Kimberly J Laverty[1], Cynthia M. Pruss[1] , Rachel M. Holden[2], Michael A. Adams[1]; Biomedical and Molecular Sciences[1] and Department of Medicine[2], Queen's University, Kingston, ON, CANADA.

63. **ASSESSMENT OF POSTNATAL CARDIAC STRUCTURE AND FUNCTION IN A SPRAGUE-DAWLEY MODEL OF CONGENITAL HEART DEFECTS.** Rebecca D. Maciver, Michael A. Adams, Louise M. Winn, & Terence R. S. Ozolinš., Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON.

64. **ASSESSMENT AND REPORTING OF SAFETY OUTCOMES IN CLINICAL TRIALS OF CANNABINOIDS FOR CHRONIC PAIN.** Mohammed M. Mohiuddin, Ian Gilron, Simon Haroutounian, Shannon Smith, Fiona Campbell, Meg Carley. From the School of Medicine, Departments of Anesthesiology & Perioperative Medicine, Biomedical & Molecular Sciences, and Centre for Neuroscience Studies, Queen's University Kingston, Ontario Canada.

65. **MEAL PHOSPHATE BIOAVAILABILITY ALTERS HORMONAL RESPONSE IN HEALTHY HUMANS.** Kathryn Neville, Mandy E Turner, Nicole Couture, Laura Couture, Cynthia M Pruss, Michael A Adams, Rachel M Holden, Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario Canada.

66. **CHARACTERIZING THE EFFECTS OF IN UTERO EXPOSURE TO VALPROIC ACID ON FETAL HEART DEVELOPMENT.** Ana Nikolovska, Louise Winn, Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

67. **MAGNESIUM FOR THE MANAGEMENT OF CHRONIC PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS.** Rex Park, BHSc, Ian Gilron, MD, MSc, FRCPC, Anthony Ho, MD, FRCPC, Meg Carley, BSc. From the School of Medicine, Departments of Anesthesiology & Perioperative Medicine, Biomedical & Molecular Sciences, and Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada.

68. **ALTERATION IN MICRO-RNA EXPRESSION PATTERN IN CD-1 MOUSE FETAL LIVER CELLS FOLLOWING IN-VITRO BENZOQUINONE EXPOSURE.** Alexander Platt[1], Louise M. Winn[1,2], [1]Department of Biomedical and Molecular Sciences, Therapeutics, Drug Development and Human Toxicology Graduate Field Queen's University, Kingston, Ontario, Canada, [2]School of Environmental Studies, Queen's University, Kingston, Ontario, Canada.

69. **INVESTIGATING THE EFFECTS OF VALPROIC ACID EXPOSURE ON PLACENTAL GROWTH AND FETAL DEVELOPMENT DURING EARLY PREGNANCY IN CD1 MICE.** *Sidra Shafique[1], Louise M. Winn[1,2].Department of Biomedical and Molecular Sciences, Queen's University, Kingston[1], School of Environmental Studies, Queen's University, Kingston[2].*

Women's and Children's Health Research

70. **VASCULAR OUTCOMES OF A PREGNANCY COMPLICATED BY PREECLAMPSIA.** Logan C Barr, Julia Herr, Claire Sumner, Jessica Pudwell, Amer M Johri, Graeme N Smith. Kingston Health Sciences Centre, Queen's University.

71. **THE EFFECT OF IN UTERO BENZENE EXPOSURE ON FETAL NF-κB CELL SIGNALLING IN CD-1 MICE.** Peter Chun Wan Lu, Louise Winn, DBMS.

72. **CARBON MONOXIDE ALTERS ENDOTHELIAL FUNCTION IN PERIPHERAL MICROVASCULATURE.** Karalyn E McRae[1], Jessica Pudwell[2], Nichole Peterson[1], and Graeme N Smith[1,2]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada and [2]Department of Obstetrics and Gynecology, Queen's University, Kingston, Ontario, Canada.

Abstracts

Biomedical Engineering

1. **DEVELOPMENT OF A VASCULARIZED CAROTID ARTERY PLAQUE PHANTOM FOR THE INVESTIGATION OF NOVEL ULTRASOUND-BASED THERAPIES.** Christie Boswell-Patterson[1], Olivia Yau[2], MSc, Stephen Pang[1], PhD, Man Yat Tse[1], PhD, Jianhua Zhou[3], PhD, Marie-France Hétu[2], PhD, Amer M. Johri[1,2], MD, MSc, FRCPC, FASE. [1] Department of Biomedical and Molecular Sciences, Queen's University. [2] Department of Medicine, Queen's University. [3] School of Engineering, Sun Yat-Sen University, Guangzhou, China.

As the global burden of atherosclerotic cardiovascular disease (ACVD) continues to rise, there is an increased demand for improved imaging techniques for earlier detection and diagnosis of atherosclerotic plaques, and for quantitative measures of disease progression. Vulnerable plaque lesions are thought to be responsible for the majority of cardiovascular events, characterized by a variety of features, including neovascularization, that increase the risk of plaque rupture and thrombosis. Contrast microbubbles can enter vulnerable plaque capillaries, allowing for their identification through contrast-enhanced ultrasound (CEUS). This project was undertaken to develop an *in vitro* model of a vascularized atherosclerotic plaque compatible with CEUS. To validate the vulnerable plaque mimic, advanced ultrasound methods were used to precisely analyze contrast agent penetration into the mimic. Greyscale Median (GSM) analysis showed significant plaque enhancement after the injection of contrast (GSM = 59.57 ± 22.46) compared with its baseline (GSM = 3.14 ± 4.6), [$p < 0.001$, n=7]. We were also able to demonstrate contrast flow through a plaque mimic, using CEUS. The neovascularized plaque phantom developed will serve as a platform for the development and validation of novel plaque imaging technologies and techniques for the investigation of plaque vascularization, risk stratification, and treatment. Overall, our findings provide a foundation for the development of a robust model of neovascularized atherosclerotic plaque, as a means to improve diagnosis and treatment of cardiovascular disease.Supported by: SEAMO (Southeastern Ontario Academic Medical Organization)Canada Foundation for Innovation, Heart & Stroke Foundation

2. **DETECTING LOW BACK PAIN FROM CLINICAL NARRATIVES USING MACHINE LEARNING APPROACHES.** Michael Judd[1], Farhana Zulkernine[1], Brent Wolfrom[2], Akshay Rajaram[2], David Barber[2]. [1] School of Computing, Queen's University, Kingston, Ontario [2] Department of Family Medicine, Queen's University, Kingston, Ontario.

Free-text clinical notes recorded during the patients' visits in the Electronic Medical Record (EMR) system narrates clinical encounters, often using 'SOAP' notes (an acronym for subject, objective, assessment, and plan). The free-text notes represent a wealth of information for discovering insights, particularly in medical conditions such as pain and mental illness, where regular health metrics provide very little knowledge about the patients' medical situations and reactions to treatments. In this paper, we develop a generic text-mining and decision support framework to diagnose chronic low back pain. The framework utilizes open-source algorithms for anonymization, natural language processing, and machine learning to classify low back pain patterns from unstructured free-text notes in the Electronic Medical Record (EMR) system as noted by the primary care physicians during patients' visits. The initial results show a high accuracy for the limited labelled data set that we used in this pilot study. We are currently processing a larger data set to test our approach

3. **DEVELOPING A SIMULATION CURRICULUM TO TEACH MEDICAL STUDENTS TO PERFORM AN ULTRASOUND-GUIDED NEEDLE INSERTION.** Sachin V. Pasricha[1,2], Zsuzsanna Keri[1], Matthew S. Holden[1], and Gabor Fichtinger[1]. [1]Laboratory for Percutaneous Surgery, School of Computing, Queen's University, Kingston, ON, Canada [2]School of Medicine, Queen's University, Kingston, ON, Canada

PURPOSE: Undergraduate medical education curricula lack consistent training for ultrasound-guided procedures.[1] We developed a simulation curriculum using augmented reality visualization to teach ultrasound-guided needle insertion on a vascular model to medical students. We measured their performance and confidence learning curves with respect to this skill. METHODS: Students participated in the four-session simulation curriculum. Prior to and after each session, each student completed a simulated ultrasound-guided needle insertion on a vascular phantom model. Probe and needle motion was electromagnetically tracked and video recorded to assess performance objectively by nine computer-generated metrics,[2] which were compared to expert benchmarks. Prior to each pre- and post-session test, students also completed a questionnaire indicating their confidence on a scale of 0-10. RESULTS: Prior to session one and post session four, 33% and 55% of students, respectively, performed at or better than the level of the expert benchmarks for at least four metrics. Prior to the simulation curriculum, 3% students had an overall confidence of 8 or higher, as compared with 72% after the curriculum. CONCLUSION: The simulation curriculum yielded marked improvement in performance and confidence. Training strategies that would benefit those students who did not meet expert benchmarks should be further investigated. **References:** 1. Kessler C, Bhandarkar S. Ultrasound training for medical students and internal medicine residents--a needs assessment. *J Clin Ultrasound.* 2010;38(8):401-408. 2. Xia S, Keri Z, Holden MS, Hisey R, Lia H, Ungi T, Mitchell CH, Fichtinger G. (2018). A learning curve analysis of ultrasound-guided in-plane and out-of-plane vascular access training with Perk Tutor. *SPIE Medical Imaging*.

4. **COMPARISON OF 3D ULTRASOUND IMAGING TO COMPUTED TOMOGRAPHY IN KNEE OSTEOPHYTE DEPICTION.** Vendries, V (MSc, BSc), Ungi, T (PhD, MD), Harry, J, Kunz, M (PhD), MacKenzie, L (PhD), Venne, G (PhD, D.O) Department of Biomedical and Molecular Sciences, Queens University.

Background: Osteophytes (marginal bony outgrowths) are a common radiographic marker of osteoarthritis[1]. However, osteophytes are not accurately depicted using conventional imaging[1,2]. This represents problems for evaluating the anatomical changes of the osteoarthritic joint, and for the design of surgical interventions that rely on the accuracy of pre-operative images[2,3]. Ultrasound is a promising tool to detect articular changes such as osteophyte presence[1,4]. Furthermore, 3D-ultrasound, a tool for volume rendering and surface representation[5], can potentially offer a means to quantify and depict osteophytes. **Objective:** To compare osteophyte depiction in the knee joint using 3D-ultrasound and conventional Computed Tomography (CT). **Methods:** Fresh-frozen-thawed human cadaveric knees were pre-scanned for the presence of osteophytes[1]. Five knee sides with were selected; 3D-ultrasound and CT images were obtained, segmented and digitally 3D-reconstructed. The knees were dissected and Structured-Light-Scanner (SLS) images of the joint surface were obtained. Surface matching and Root-Mean-Square-Error (RMSE) analyses were performed to assess the accuracy of each of the evaluated modalities in capturing the anatomy at the sites of osteophytes. 3D-ultrasound and CT models were compared to the SLS model, which was used as ground truth. **Results:** The average RMSE for 3D-ultrasound-to-SLS and for CT-to-SLS model comparisons were 0.87mm and 0.95mm respectively ($p=0.43$). Comparative observation of imaging modalities set against each other suggests that 3D-ultrasound is superior in depicting osteophytes with cartilage and fibrocartilage tissue characteristics compared to CT.

5. **AN EDGE COMPUTING FRAMEWORK TO RECEIVE AND PROCESS STREAMING WEARABLE SENSOR DATA FOR PATIENT MONITORING.** Dharmitha Ajerla. Sazia Mahfuz, Farhana Zulkernine, School of Computing

With the rising cost of healthcare, and increase in elderly population and chronic diseases, there is an urgent need to change the approach to healthcare from generic to personalized health monitoring with a goal to reducing healthcare expenses and improving life-style. The general population are increasingly becoming more health conscious as evident from the increasing use of wearable sensor devices like Fitbit. Some of these devices measure activities ranging from steps taken to oxygen levels in the body. Usually data from these devices are uploaded and processed on the cloud by a linked mobile device like a smartphone that is supported by the device manufacturer. As a result, real-time patient monitoring is not only expensive but also impossible using these expensive devices. We are developing an edge computing framework to enable real-time patient monitoring at caregiving institutions and clinics using much cheaper sensor devices and a nearby edge device like a laptop. In addition, we have already developed a Long Short-Term Memory neural network model to predict casualties such as fall using a published web dataset called "MobiAct" having an accuracy of 95%, which we will now apply to the real-time patient monitoring data.

Cancer Research

6. **THE IMPACT OF NAT1 GENETIC POLYMORPHISM ON CATALYTIC ACTIVITY IN THE HUMAN COLON MUCOSA.** Griffin Pauli, Sandra Graham, Dr. Thomas Massey, Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada

Colorectal cancer (CRC) incidence remains among the highest of all cancers in Canada. Notably, increasing evidence suggests the diet may play an important role in pathogenesis. There is an accumulating body of evidence linking a positive association between intake of compounds in cooked red meats and CRC risk. Specifically, heterocyclic aromatic amines (HAAs), such as 2-amino-1-methyl-6-phenylaimidazo-(4,5-pyridine) (PhIP), have been implicated as they demonstrate a high degree of mutagenicity in bacterial assays and induce tumour formation *in vivo*. The metabolic pathway for relevant HAAs involves phase I hydroxylation and phase II conjugation to acetyl CoA catalyzed by N-acetyltransferase 1 and 2 (NAT1/NAT2). Acetylation by the NATs produces electrophilic N-acetoxy-HAA species which bind DNA forming bulky adducts, possibly causing mutations if not repaired. Polymorphism in the NATs has been shown to modulate the catalytic activity and subsequent bioactivation of HAAs to genotoxic products. The present study was conducted to validate the NAT1 activity assay used in determining catalytic activity and to investigate the impact of polymorphism on NAT1 activity. Results demonstrated the NAT1 activity assay functions to accurately characterize NAT1 enzyme activity. Further, early results demonstrate an unexpected genotype-phenotype relationship. Specifically, samples possessing the NAT1*10 allele, belonging to the intermediate/rapid genotype, did not display significantly increased acetylation activity. As consumption of red meat is modifiable lifestyle factor, understating the mechanisms behind genetic susceptibility is crucial. (Supported by the Cancer Research Society

7. **CLASSIFYING PATHWAYS TO THE DIAGNOSIS OF COLORECTAL CANCER: A NEW APPROACH USING ADMINISTRATIVE DATA IN ONTARIO.** Zhen Guan1,2, Colleen Webber2, Jennifer Flemming2, Bingshu Chen3, Patti Groome1,2 Department of Public Health Sciences, Queen's University, Kingston, ON, Canada Division of Cancer Care and Epidemiology, Queen's Cancer Research Institute, Queen's University, Kingston, ON, Canada Canadian Cancer Trials Group, Queen's University, Kingston, ON, Canada

Objectives-The objective of this study is to describe the diagnostic pathways in colorectal cancer (CRC) in Ontario through the development of a pathway categorization scheme. Methods This study used an existing cohort at ICES which holds numerous administrative and registry data that can be used by authorized researchers with appropriate approvals. The cohort included patients who were diagnosed with CRC in Ontario between 2009 and 2012. Eleven variables that were related to patient presentation, patient visit pattern and patient procedures were used to categorize diagnostic pathways. Two-step cluster analysis was conducted given the mixed type of variables. Results Six clusters were identified based on statistical criteria and clinical assessments. 94% patients in Cluster 1were diagnosed through screen-detected route. 86% patients in Cluster 2 had colonoscopies, but only 30% of them had imaging tests as the first procedure, compared to 70% patients in Cluster 6. 44% patients in Cluster 4 were diagnosed through the ED compared to 12% in Cluster 5. But they were all more likely to had imaging tests first rather than colonoscopies. Patients in Cluster 3 had no procedures with 38% presenting in the ED. Conclusions Variations between the clinical and the recommended pathways were revealed. The next step of this study is to examine the difference between these groups in terms of patient, disease, and system-related factors.

8. **THE ROLE OF FUCOSYLATION ON SPHEROID FORMATION FROM CHEMORESISTANT PROSTATE CANCER CELLS**. Regina-Veronicka Kalaydina, Hedi Zhou and Myron R Szewczuk. Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

Aberrant cell surface modifications involving glycosylation have been linked to a variety of cancers including prostate cancer (PCa), which affects roughly 1.1 million people worldwide. Fucosylation is a type of cell surface glycosylation that involves the transfer of a fucose to a substrate, with overexpression of α-1,6 fucose having been detected in aggressive PCa. With the growing use of multicellular tumor spheroids (MTS) to study complex interactions in the tumor microenvironment (TME), prostate spheroids constitute a good three-dimensional *in-vitro* model. Prostate spheroids have been generated from DU145 PCa cells and their Gemcitabine-resistant (GemR) variants using the cyclo-RGDfK(TPP) peptide, which has been reported to accurately recapitulate the TME. Evidence from immunocytochemistry stains using biotinylated lectins that block α-1,6 and α-1,2 fucose linkages indicates that the DU145 and DU145GemR cells possess unique fucose expression profiles. Additionally, pre-treating prostaspheres generated from DU145 and DU145GemR with lectins that block α-1,6 fucose reduces spheroid formation. Thus, in addition to the previously established role of sialylation in MTS formation, fucosylation may contribute to prostate spheroid formation using cyclo-RGDfK(TPP). The role of glycosylation in tumor spheroid formation is an emerging yet poorly understood area of research that can enhance our understanding of the mechanisms behind tumor growth in humans. The present study sheds light on whether fucosylation differs between chemoresistant cells and their non-chemoresistant counterparts in prostate cancer, which can aid in improving our understanding of fucosylation and how it relates to chemoresistance.

9. **INTERLEUKIN-27: A POTENTIAL CYTOKINE TO COMBAT AGGRESSIVE METASTATIC PROSTATE CANCER?** Olena Kourko[1], Daniela Cino[1], Robin Smyth[1], Carlene Petes[1], Kyle Seaver[1], Natalya Odoardi[1], Sameh Basta[1], Katrina Gee[1] [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, K7L 3N6

Interleukin(IL)-27 is a heterodimeric cytokine that links innate and adaptive immunity, and shows potential as a therapeutic agent in tumour immunotherapy for a variety of different cancers, including prostate cancer. Prostate cancer is the most common type of cancer affecting men in Western Countries. In Canada, prostate cancer is the third leading cause of death from cancer in men. The tumour complexity and heterogeneity creates challenges in treating prostate cancer. Immunotherapies have shown great success in targeting and treating various cancers in patients; however, despite advances in cancer therapeutics, no curative treatment is available for metastatic prostate cancer. TLR3, a member of the transmembrane toll-like receptors family, has been suggested to be involved in apoptosis of prostate cancer cells. Thus, we decided to trigger TLR3 activation in prostate cancer cell lines with poly(I:C), a synthetic, double-stranded RNA TLR3 agonist. When delivered alone, poly(I:C) did not cause significant death; however, simultaneous addition of IL-27 caused significant cell death. How IL-27 increases the ability of poly(I:C) to cause cell death in these metastatic, aggressive cancer cells is unknown, but our data show that IL-27 modulates expression levels of TLR3 in prostate cancer cell lines. Taken together, our results suggest that IL-27 should be explored further in therapeutic immunotherapy of targeting and effectively treating aggressive cancers. This work was funded by the Prostate Cancer Fight Foundation and Motorcycle Ride for Dad

10. **ROLE OF THE PROGRAMMED DEATH LIGAND 1 (PD-L1) IMMUNE CHECKPOINT IN THE ACQUISITION OF MALIGNANT PHENOTYPES IN TUMOUR CELLS** Minassian L[1,2], Sanwalka D[1,2], Macdonald-Goodfellow S[1,2], Ghaffari A[1,2], Craig A, Siemens[1,2,3] DR, Graham CH[1,2,3] *1) Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada. 2) Cancer Research Institute, Queen's University, Kingston, Ontario, Canada. 3) Department of Urology, Kingston General Hospital, Kingston, Ontario, Canada.*

Most studies on the Programmed Death 1 (PD-1)/Programmed Death Ligand 1 (PD-L1) immune checkpoint have focused on elucidating the signalling mechanisms leading to inactivation of immune effectors. There is evidence that signalling by the PD-1/PD-L1 immune checkpoint may be bidirectional, and we have shown that reverse signalling by PD-1/PD-L1 leads to activation of oncogenic pathways as well as resistance to chemotherapeutic agents in tumour cells. Autophagy is a well-established mechanism of chemoresistance in cancer cells. Hence, we hypothesized that PD-1/PD-L1 signaling induces chemoresistance in tumor cells by up-regulating autophagic pathways. Conversion of microtubule-associated protein light chain 3 (LC3)-I to LC3-II is a requirement for autophagosome formation and is a robust marker of autophagy. Immunoblot analysis demonstrated that exposure of human breast cancer cells to recombinant PD-1 (rPD-1) resulted in a time-dependent increase in LC3-II as well as Beclin-1, another mediator of autophagy. Treatment with rPD-1 also resulted in increased recruitment of LC3-II to the autophagic membrane. Moreover, imaging studies using live breast cancer cells expressing GFP-tagged LC3 revealed a time-dependent increase in autophagosome formation following administration of rPD-1. Using inhibitors of autophagy, we are currently investigating whether drug resistance induced by reverse PD-1/PD-L1 signalling is causally linked to increased autophagy. These studies provide a rationale for the use of PD-1/PD-L1 immune checkpoint blockers as potential chemosensitizers in cancer therapy. (Supported by CIHR)

11. **IDENTIFYING BIOMARKERS OF RESPONSE TO WEE1 INHIBITOR (AZD1775) AND ITS EFFECT ON THE TUMOUR IMMUNE MICROENVIRONMENT IN HIGH-GRADE SEROUS OVARIAN CANCER.** Sarah Nersesian, Nichole Peterson, Julie Ann-Francis, Carlos Escobedo and Madhuri Koti

Ovarian cancer is the leading cause of gynecological malignancies in the world. Patients with high grade serous ovarian cancer (HGSC) exhibit high rates of resistance to conventional platinum based chemotherapy that leads to poor overall survival rates. Almost 50% of HGSC tumors are deficient in genes associated with DNA damage repair (DDR) and over 96% of these tumors are mutated in *TP53*, a G1 cell cycle checkpoint protein. Upon DNA damage these tumors heavily rely on G2 phase checkpoint proteins, including Wee1. Inhibition of Wee1 by AZD1775 has demonstrated the ability to sensitize p53 deficient tumors to DNA damaging agents. The importance of the immune system in response to chemotherapy is well established and our findings from HGSC tumours provides evidence linking DDR and tumor intrinsic alterations in the Type 1 interferon (IFNI) pathways that modulate the tumor immune microenvironment towards differential response to chemotherapy. This study aims to identify predictive biomarkers of response to AZD1775 and the impact of pre-existing tumor immune microenvironment on therapeutic efficacy. We will evaluate the efficacy of AZD1775 alone and in combination with platinum based chemotherapy and paclitaxel using syngeneic ID8 mouse model in immune competent C57/BL6 mice. In vitro studies will be conducted in a panel of genetically distinct HGSC cell lines. Findings will facilitate precise use of AZD1775 in combination with chemotherapy and/or current immune based therapies. This study is supported by funding from Queen's University and AstraZeneca.

12. **AUTOPHAGY IS REQUIRED FOR TUMOUR CELL DRUG RESISTANCE INDUCED BY THE PROGRAMMED DEATH LIGAND 1 (PD-L1) IMMUNE CHECKPOINT.** Sanwalka, D.[1], Minassian L.M.[1], Sutherland, L.[1], MacDonald-Goodfellow S.[1], Ghaffari, A.[1], Koti, M.[1], Siemens, D.R.[1,2] and Graham, C.H.[1,2] 1. Department of Biomedical and Molecular Sciences, Queen's University 2. Department of Urology, Kingston General Hospital

Most studies on the Programmed Death 1 (PD-1)/Programmed Death Ligand 1 (PD-L1) immune checkpoint focus on elucidating signalling mechanisms leading to inactivation of immune effectors. We have shown that binding of PD-1 to PD-L1 on the surface of tumour cells leads to activation of oncogenic pathways as well as resistance to chemotherapeutic agents in the tumour cells. Autophagy is a well-established mechanism of drug resistance in cancer cells. Hence, we hypothesized that PD-1/PD-L1 signaling induces drug resistance in tumor cells by up-regulating autophagic pathways. Immunoblot analysis demonstrated that exposure of human breast cancer cells to recombinant PD-1 (rPD-1) resulted in a time-dependent increase in LC3-II as well as Beclin-1, two important mediators of autophagy. 4T1 mammary carcinomas from mice treated with rPD-1 also had increased levels of LC3-II. Moreover, imaging of live breast cancer cells expressing GFP-tagged LC3 revealed a time-dependent increase in autophagosome formation following administration of rPD-1. Using inhibitors of autophagy, we have shown that drug resistance induced by reverse PD-1/PD-L1 signalling is causally linked to increased autophagy. These studies provide a rationale for the use of PD-1/PD-L1 immune checkpoint blockers and autophagy inhibitors as potential chemosensitizers in cancer therapy. Supported by the Canadian Institutes of Health Research and the Terry Fox Research Institute

13. **EVALUATING THE EFFICACY AND IMMUNOGENICITY OF A PROPHYLACTIC CANCER VACCINE.** Kyle Seaver[1], Peter Greer[2] and Sam Basta[1]. [1]Department of Biomedical & Molecular Science Queen's University, Kingston, Ontario, Canada. [2]Division of Cancer Biology and Genetics, Cancer Research Institute, Department of Pathology and Molecular Medicine, Queen's University, Kingston, Ontario, Canada.

Conventional cytotoxic therapies are primary treatment options for cancer patients; however, these therapies can be associated with toxicity, drug resistance, and immune cell depletion. In turn, there is a need for alternative therapies, which has led to increased attention towards cancer immunotherapies. Prophylactic cancer vaccines represent an avenue of research within the field of cancer immunotherapy that focuses on proactive and early intervention and aim to initiate an antitumour immune response prior to the development of immune escape mechanisms. The goal of my research is to evaluate how a prophylactic vaccination model can provide protection against tumorigenesis *in vivo.* In this study we compare different protocols for tumour cell vaccine preparation in combination with vaccine adjuvants to develop an antitumour immune response. The basis for this work is that cancer vaccines, combined with novel adjuvants, will enhance tumour antigen presentation and T cell activation. Our findings demonstrate that the mode of cell death in combination with CpG can have a major influence on the development of an anti-tumour immune response that reduces cancer progression. This data provides the necessary foundation to study prophylactic cancer vaccination models that can subsequently include other adjuvants in combination with CpG, while laying the foundation to better understand tumour immune cell interactions. Ultimately, this research will provide further evidence for developing preventative cancer therapies while helping improve current cancer immunotherapies. (Terry Fox Foundation, Training program in Transdisciplinary Cancer Research).

14. **REGIONS CONNECTING THE MEMBRANE SPANNING AND NUCLEOTIDE BINDING DOMAINS OF MULTIDRUG RESISTANCE PROTEIN 1 (MRP1) ARE FUNCTIONALLY DISTINCT**. Emma E. Smith, Gwenaëlle Conseil and Susan P. C. Cole,Department of Pathology and Molecular Medicine

The MRP1/ABCC1 transporter confers multidrug resistance by reducing intracellular drug accumulation through active efflux across the plasma membrane. MRP1 also effluxes xeno- and endobiotic organic anions that include estradiol glucuronide ($E_2$17βG) and leukotriene C_4 (LTC_4). MRP1 has three membrane spanning domains (MSD) that form the solute translocation pathway, and two nucleotide binding domains (NBD) which bind and hydrolyse ATP. MSD1/2 are linked to NBD1/2 by connecting regions (CR) 1 (aa 600-642) and CR2 (aa 1249-1291), respectively. To test the hypothesis that the CRs have distinct roles in MRP1 structure and function, Ala substitutions of eight conserved CR1 and CR2 residues were generated. Cellular levels of three of four CR1 mutants (S612A, R615A, E624A) were lower than wild-type MRP1 (by 60%, 95%, 95%, respectively; $p<0.05$). Of the four CR2 mutants, only W1287A cellular levels were markedly reduced (by 80%; $p<0.05$). A bovine Mrp1 cryo-EM structure suggests that some mutation-sensitive residues may participate in stabilizing interactions. This idea was not supported by the characterization of double exchange mutants, which failed to restore MRP1 levels. For CR mutants expressed at levels similar to wild-type MRP1, only CR2-G1291A exhibited a substrate-selective change in [^{3}H]LTC_4 transport (reduced by 40%; $p<0.05$) whereas [^{3}H]$E_2$17βG transport was unaffected. Our results suggest that CR1 is more important than CR2 for stable MRP1 expression, whereas CR2 may play a larger role in MRP1 function. Supported by CIHR grant MOP-133584

15. **A PHARMACOGENOMICS ANALYSIS OF BIOLOGICAL NETWORKS REGULATING CHEMOTHERAPY RESPONSE AMONG OVARIAN CANCER PATIENTS.** Danai G. Topouza[1], Jihoon Choi[1], Sean Nesdoly[2] and Qingling Duan[1,2]. [1]Department of Biomedical and Molecular Sciences, Queen's University [2]Queen's School of Computing, Queen's University Kingston, Ontario, Canada.

Ovarian cancer has the lowest survival rate of all common gynaecological cancers. The gold standard of care for ovarian cancer is surgery and platinum-based chemotherapy; however, more than a third of patients are not responsive to this treatment. The underlying mechanism of platinum therapy resistance remains poorly understood. In this study, I analyzed sequence data from 190 ovarian cancer patients to detect gene expression networks and genomic variants associated with platinum chemotherapy response. I have developed a bioinformatics pipeline capable of processing patient RNA-seq data, and producing genome and transcriptome information for each patient. The aims of this project are to: (i) identify differentially expressed genes using univariate analysis; (ii) identify and characterize gene co-expression networks using multivariate analysis; and (iii) associate patient genomic variants with platinum chemotherapy response. Characterizing genes and networks associated with therapy response will implicate the underlying platinum therapy resistance mechanisms. Understanding these mechanisms can increase the efficacy of future medication by providing novel drug targets. Additionally, the successful association of genomic variants with platinum therapy resistance will provide genetic markers for patient screening. These markers can be used to identify chemotherapy non-responders as potential candidates for combinatorial therapies. The results of this study will therefore aid in the development of effective and personalised approaches to ovarian cancer therapy.

16. **STAT1 EXPRESSION ASSOCIATES WITH PD-L1 AND IDO1 IMMUNE CHECKPOINT GENE EXPRESSION IN HIGH-GRADE SEROUS OVARIAN CANCER.** Thiago Vidotto, Nichole Peterson, Barbara Vanderhyden, Manon de Ladurantaye, Anne-Marie Mes-Masson, Julie-Ann Francis, Madhuri Koti. Department of Biomedical and Molecular Sciences, Queen's University.

High-grade serous ovarian cancer (HGSC) patients show dismal survival rates and have not benefited from immune checkpoint-based therapies. We previously showed that interferon (IFN)-induced Signal Transducer and Activator of Transcription (STAT1) is a chemotherapy response predictor as well as a prognostic biomarker in HGSC. STAT1 expression also significantly correlated with $CD8^+$ tumour infiltrating lymphocyte (TIL) density in pre-treatment HGSC tumours. Chronic IFN signaling in cancer promotes inflammation, immunosuppression and an aggressive disease. We thus hypothesized that increased IFN-γ from a pre-existing T_H1 type immune response may induce expression of immune checkpoint genes and eventual adaptive immune resistance. We conducted whole transcriptome sequencing of RNA from 60 HGSC tumours with known STAT1 gene/protein expression levels and $CD8^+$ TIL density. R Bioconductor DESeq based RNA-sequencing data analysis showed a total of 570 differentially expressed genes between tumors with high (n=32) and low (n=28) STAT1 expression (adjusted $P<0.01$). Gene Ontology and KEGG enrichment analysis showed an enrichment of genes associated with type I IFN signaling pathway, viral-associated immune response, antigen processing and presentation, and innate immunity. Importantly, we also observed significantly higher expression levels of *PD-L1* and *IDO1* genes in the high STAT1 group indicating possible evolution of adaptive immune resistance. These results were independently validated in 379 HGSC tumors from The Cancer Genome Atlas (TCGA). Findings from this study suggest that HGSC patients, identified as cold tumours due to decreased expression of STAT1 and low $CD8^+$ TIL density, will potentially benefit from immune checkpoint blockade therapy via sensitization using immune priming based combination treatment approaches. Funding for this study was provided by the Nancy Sutherland Fund for Promotion of Knowledge in Ovarian Cancer. Thiago Vidotto is supported by scholarship from São Paulo Research Foundation (FAPESP).

17. **LOSS OF PTEN DECREASES THE PROSTATE CANCER CELL-INTRINSIC TYPE I INTERFERON RESPONSE.** Natasha Vitkin1, Nichole Peterson2, D. Robert Siemens3, Madhuri Koti1,2,4 1) Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada. 2) Division of Cancer Biology and Genetics, Queen's University, Kingston, Ontario, Canada. 3) Department of Urology, Queen's University, Kingston, Ontario, Canada. 4) Department of Obstetrics and Gynecology, Queen's University, Kingston, Ontario, Canada.

Prostate cancer (PCa) is the 2nd most commonly diagnosed cancer in Canadian men. Loss of the tumor suppressor gene *phosphatase and tensin homolog (PTEN)* occurs in 15-30% of PCa tumors and is associated with disease progression and aggressive phenotype. Clinical and preclinical studies demonstrate that loss of PTEN expression correlates with decreased Type I Interferon (IFN1) pathway genes, suggesting that PTEN augments the cellular immune response. We generated *PTEN* knockout derivatives of PCa cells using CRISPR to determine the role of PTEN in shaping cellular immune-related properties and response to IFN1 stimulations. Our results revealed statistically significant differences in expression patterns of IFN1 pathway genes in *PTEN*-knockout cells during normal growth and following treatment with IFN1 agonists. Genes involved in innate immune signaling, antiviral responses, and inflammation were significantly decreased in *PTEN*-knockout cells. Additionally, *PTEN*-knockout cells had significantly decreased secreted levels of major inflammatory and chemotactic cytokines including IL-8 and CXCL1 compared to *PTEN*-intact PCa cells. Given the significance of the cross-talk between cancer cells and surrounding immune cells in cancer progression, these findings are important in elucidating the specific contribution of cell-intrinsic pathways to the PCa tumor microenvironment. This investigation may lead to exploitation of PCa cell-intrinsic IFN1 pathways for rational design and use of immune-based therapies to improve management of PCa. *Supported by Prostate Cancer Canada, The Terry Fox Research Institution, and Canadian Institutes of Health Research.*

18. **MICRORNA-BASED CLASSIFICATION OF GASTROINTESTINAL NEUROENDOCRINE TUMORS**. Justin Wong[1], Nicole Panarelli[2], Kathrin Tyryshkin[1], Adrianna Majewski[1], Xiaojing Yang[1], Theresa Scognomaglio[2], Michelle Kim[3], Kimberley Bogardus[4], Thomas Tuschl[4], Yao-Tseng Chen[2], Neil Renwick[1,4]. [1]Laboratory of Translational RNA Biology, Queen's University, Kingston, ON, Canada; [2]Department of Pathology and Laboratory Medicine, Weill Cornell Medical College, New York, NY, USA; [3]Center for Carcinoid and Neuroendocrine Tumors of Mount Sinai, Icahn School of Medicine at Mount Sinai, New York, NY, USA; [4]HHMI_Labratory of RNA Molecular BIology, The Rockefeller University, New York, NY, USA

Gastrointestinal Neuroendocrine Tumors (GI-NETs) can be challenging to evaluate histologically. microRNAs (miRNAs) are small regulatory RNA molecules that can be used as biomarkers due to their abundance, cell-type and disease-stage specificity, and stability. Recent advances in miRNA detection, sequence annotation, and data mining techniques facilitate using miRNA profiling to compliment histological evaluation of NETs. To evaluate miRNAs as markers for classifying and grading GI-NETs, we generated and compared miRNA expression profiles from pancreatic, ileal, appendiceal, and rectal NETs using barcoded small RNA-seq. Following data preprocessing, we manually assigned sample profiles to discovery (80%) and validation sets (20%) prior to data mining using machine-learning techniques. Leveraging prior knowledge that GI-NET behavior is influenced by embryonic derivation, we developed and assessed the accuracy of a dual layer classifier for differentiating GI-NET types. In the first layer, our classifier discriminated between midgut (ileum, appendix) and non-midgut (rectum, pancreas) NETs based on miR-615 and -92b expression. In the second layer, our classifier discriminated between ileal and appendiceal NETs based on miR-125b, -192 and -149 expression, and between rectal and pancreatic NETs based on miR-429 and -487b expression. This approach classified GI-NET sites with overall accuracies of 98.5% and 94.4% in the discovery and validation sets, respectively, and has the potential to be used alongside morphological and immunohistochemistry-based approaches.

19. **REGULATION OF DIFFERENTIATION OF BALB/C3T3-DERIVED PREADIPOCYTES BY CRAC1.** Veronica Youssef, Stephanie Guy, Yichang Huang, Evangelia Tomai, Leda Raptis

It was previously demonstrated that the differentiation of established preadipocytes requires confluence and stimulation with insulin and Dexamethasone inducers. Cadherin-11 engagement, which is favored under conditions of confluence, increases the levels and activity of the Rac small GTPase in mouse Balb/c-3T3 fibroblasts, as well as preadipocytes derived from them. To test the involvement of cRac1 upon adipocytic differentiation, cells were treated with specific inhibitors or anti-sense RNA expression. The results demonstrated that Rac is required for adipocytic differentiation, especially at a narrow window of time before differentiation has been induced through insulin and Dexamethasone addition. To further investigate the functional relationship between the transforming ability of Rac and its role as an integral component of the differentiative cadherin signaling pathway, we introduced a mutationally activated form of Rac, Rac^{V12}-GFP, into a preadipocytic line derived from Balb/c3T3 cells. Our results demonstrate that, in the absence of the inducers, Rac^{V12}-GFP expression increased adipocytic differentiation, indicating that Rac^{V12}-GFP can potentiate or replace the insulin differentiative signal. In the presence of the inducers however, Rac^{V12}-GFP reduced differentiation. Interestingly, the Rac^{V12}-GFP- expressing cells were not fully transformed, as shown by their inability to grow under anchorage independent conditions. Taken together, these findings indicate that activated Rac can block adipocytic differentiation in the absence of full neoplastic conversion.

20. **DIFFERENTIAL PHOSPHORYLATION OF THE SIGNAL TRANSDUCER AND ACTIVATOR OF TRANSCRIPTION-3 (STAT3) AND THE DOMINANT-NEGATIVE MUTANT STAT3β, FOLLOWING CADHERIN ENGAGEMENT *VS* EXPRESSION OF ACTIVATED SRC^{527F}.** Veronica Youssef, Zaid Taha, Mulu Geletu, Leda Raptis

Stat3 is activated by receptor and non-receptor tyrosine kinases and plays an etiological role in neoplasia. Stat3 activation entails phosphorylation at tyr-705, Stat3 dimerization through a reciprocal, SH2 domain-phosphotyrosine interaction, nuclear translocation and transcription of genes involved in cellular survival (survivin, Bcl-xL). Full-length Stat3 (termed Stat3α) has an SH2 domain, tyr-705 and a carboxy-terminus encoding the transcription activation domain (TAD). Stat3β is a naturally-occurring splice variant which is lacking TAD. Therefore, Stat3β dimerizes with Stat3α but is defective in transcriptional activation, resulting in inhibition of Stat3α function. Src activates the E2F transcription factor family, which targets genes of cell proliferation, but also apoptosis. Activation of survival proteins such as Stat3α inhibits E2F-induced apoptosis, resulting in a net effect of increased cell division. Since the sequences around tyr705 are identical, we examined the phosphorylation pattern in Stat3α *vs* Stat3β. Our results demonstrate that confluence results in phosphorylation of Stat3α-705 preferentially, despite the fact that this site is present in both isoforms. In sharp contrast, activated Src^{527F} expression results in phosphorylation of both Stat3α and Stat3β equally. This feedback loop that reduces the activity of Stat3α triggers apoptosis of Src^{527F}-expressing cells preferentially, because of their high E2F levels. As a result, any tumor cells that naturally express high Stat3β levels would be very sensitive to pharmacological Stat3 inhibition, a finding which could have significant therapeutic implications.

Cardiac, Circulatory, and Respiratory Science

21. **THE IMPACT OF ISOMETRIC HANDGRIP TRAINING (IHGT) ON CARDIOVASCULAR REACTIVITY TO ACUTE MENTAL STRESS**. Kaitlyn R. Liu, Sarah E. Bailey, Morgan D. Silvester, Kyra E. Pyke, Queen's University, Kingston, Ontario, Canada, School of Kinesiology and Health Studies (Cardiovascular Stress Response Lab)

Introduction: High cardiovascular stress reactivity is associated with elevated cardiovascular risk and aerobic exercise training may reduce reactivity. While there is growing evidence that isometric handgrip training (IHGT) can reduce resting blood pressure (BP) in both normotensive and hypertensive adults, the impact of IHGT on cardiovascular stress reactivity has been minimally studied. Purpose: to investigate the impact of IHGT on cardiovascular reactivity, in response to an acute mental stress task. Hypothesis: the training group will exhibit reduced cardiovascular reactivity, compared to the control group. Methods: 20 young (22 ± 3.6 years) healthy, normotensive males were randomized to either control or training group. Training consisted of an 11min handgrip exercise session performed 5 days/week for 5 weeks. Participants completed a pre- and post-intervention visit. Cardiovascular reactivity, defined as changes in BP and heart rate (HR), was measured in response to an acute mental stress task that included a speech and mental arithmetic. Results: no significant difference in HR ($p = 0.66$) or BP (MAP: $p = 0.61$, SBP: $p = 0.68$, DBP: $p = 0.51$) reactivity was exhibited between the control and training group. Conclusion: this research suggests that IHGT does not alter cardiovascular reactivity to acute stress in young, healthy males. This is in contrast to findings in older, hypertensive adults, suggesting that the impact of IHGT on cardiovascular reactivity may be population specific.

22. **MECHANICAL STRETCH STIMULATES THE ACTIVITY OF POTASSIUM CHANNEL KV1.5.** Alexandria Milton, Wentao Li, Jun Guo, Shawn Lamothe, and Shetuan Zhang, Department of Biomedical and Molecular Sciences, Queen's University.

Cardiomyocytes continuously undergo mechanical load. During diastole of the cardiac cycle, blood fills the cardiac chambers and stretches the cardiomyocytes, a pathway that can be influenced by increased blood pressure and fluid retention. The cardiac voltage-gated potassium channel Kv1.5, generates the ultra-rapid delayed rectifier current (I_{Kur}). Hypertension and cardiac dilation cause atrial fibrillation, an arrhythmia linked to Kv1.5 dysfunction, therefore we aim to study the effects of mechanical stretch on Kv1.5 channel function. To study the effect of mechanical force on Kv1.5 channels, we used whole-cell voltage clamp and Western blot analysis in human embryonic kidney cells stably expressing Kv1.5. Low speed centrifugation (62 X g, 5 min) and low extracellular osmolarity (0.67 of normal cell culture medium; or 213 vs 320 osmolarity) were used to simulate an increase in mechanical force. Our data showed that both low-speed centrifugation for 5 min and low osmolarity treatment of cells for 60 min significantly increased Kv1.5 currents. It was demonstrated that cell swelling increased mature Kv1.5 channel density and co-IP experiments indicated that the membrane protein integrin associated with Kv1.5. Inhibition of focal adhesion kinase (FAK) with a selective inhibitor (FAK inhibitor 14) abolished cell swelling-induced increase in Kv1.5 expression and current. Our finding provides insights into the linkages between mechanical forces and electrical activities in the heart, and a novel mechanism for atrial dilation-associated atrial fibrillation.

23. **DEVELOPMENT OF A CARDIAC ULTRASOUND LEARNING MODULE TO ENHANCE THE TEACHING OF ANATOMY IN MEDICAL SCHOOLS**. Salwa Nihal, Joshua N. Durbin, Terry Li, Abbas Rizvi, Stephen C. Pang and A.M. Johri. Department of Biomedical & Molecular Sciences and Division of Cardiology, Department of Medicine, Queen's University.

Ultrasound (US) is one of the most important initial diagnostic and therapeutic tools in cardiovascular medicine. Advancements in this technology have succeeded in the development of more portable, accessible and cost effective devices such as point-of care ultrasound (POCUS), which are gaining popularity in every specialty of medicine. Due to increasing popularity of US in the medical field, in the future there is a strong likelihood that physicians including general practitioners will encounter such devices in their clinical practice. Hence, it seems timely to introduce US technology in preclinical medical education. The primary purpose of this research was to develop a module with basic introduction to US technology in the form of echocardiogram. It is hope that this learning module can enable students to establish a correlation between two dimensional images of echocardiogram and three dimensional images of cadaveric hearts dissected in the same planes as in US. After the establishment of the learning module and to determine the validity of this learning tool, quantitative and qualitative analyses were performed. A total of 100 first-year medical students from Queen's University School of Medicine were recruited in this study; they were randomly assigned into two groups with 50 students per group. The first group (Test) was presented with the learning module in the form of an US tutorial with images of cadaveric specimens while the second group (Control) was given the same tutorial but with traditional illustrated images taken from textbooks. Both groups performed a pre-test before, and a post-test and survey after the tutorial. The quantitative data collected via the post-test failed to show a significant difference between the two groups in terms of their anatomical knowledge. However, the qualitative data collected from the survey indicate that this learning module was well received by the students. Students showed great desire and enthusiasm in learning the US imaging technique early in their medical education. This pilot study can be a stepping stone for Queen's University to consider complementing imaging technologies including US during the gross anatomy components of early undergraduate medical education.

24. **NATURAL KILLER CELL HOMEOSTASIS, INTERLEUKIN-15 AND TRANSFORMING GROWTH FACTOR-β SIGNALING IN THE CHRONIC HYPOXIA MOUSE MODEL OF PULMONARY ARTERIAL HYPERTENSION.** Matthew T. Rätsep[1], Rhiannon Hilton[2], Melissa Mitchell[2], Maureen O'Connor-McCourt[3], and Mark L. Ormiston[1,2], Departments of Medicine[1] and Biomedical and Molecular Sciences[2], Queen's University, Kingston, Ontario, Canada and Formation Biologics Inc.[3], Montreal, Quebec, Canada.

Pulmonary arterial hypertension (PAH) is a disease of chronic obstructive lung vascular remodeling, which causes increased cardiac stress and eventual death by heart failure. We have shown that natural killer (NK) cells are reduced in number and impaired in function in PAH patients. Intracellular signaling mechanisms mediating this NK cell impairment and loss are unknown. Using the chronic hypoxia mouse model of PAH, we interrogated interleukin (IL)-15 and transforming growth factor (TGF)-β signaling, well-established homeostatic regulators of NK cell survival, proliferation, and function. Mice (8-12 wks) were exposed to chronic hypoxia (10% O_2) or room air (21% O_2) for 2 weeks. One group of mice received a single dose (0.5μg) of IL-15 or vehicle control. In a separate cohort, mice were treated twice weekly with AVID200 (5mg/kg), an isoform-selective TGF-β ligand trap, or IgG control. We used flow cytometric assays to determine NK cell numbers, surface marker expression, intracellular signaling, and function in blood, spleen, and lungs. Chronic hypoxia reduced circulating NK cell number, but did not affect other lymphocyte subsets. IL-15 treatment expanded NK cells in normoxia, but this response was blunted in hypoxia. AVID200 treatment partially blocked hypoxia-induced NK cell decline. NK cell intracellular signaling was similar between normoxia and hypoxia. These data suggest hypoxia-induced NK cell decline may not be caused by the actions of extrinsic factors, such as TGF-β or IL-15. Supported by the Canadian Institutes of Health Research, the Canada Research Chairs Program, and the Department of Medicine John Alexander Stewart Fellowship.

25. **DIFFERENTIAL REGULATION OF HERG CURRENT AND EXPRESSION BY ACTIVATION OF PROTEIN KINASE C.** Morgan Sutherland-Deveen, Jun Guo, Wentao Li, Jihang Yu, Shawn M. Lamothe, and Shetuan Zhang, Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada.

The *human ether-à-go-go-related gene* (*hERG*) encodes the pore-forming alpha subunit of the channel that conducts the rapidly activating delayed rectifier potassium current (I_{Kr}) in the heart. Reductions in I_{Kr} cause long QT syndrome, which predisposes individuals to potentially fatal arrhythmias that can be triggered by stress. One link between stress and hERG function is protein kinase C (PKC) activation. However, the effects of PKC activation on hERG channels are complex and seemingly conflicting results have been reported. In the present study, we investigated both acute and chronic effects of PKC activation using phorbol 12-myristate 13-acetate (PMA) on hERG channels expressed in human embryonic kidney (HEK) 293 cells. We show that chronic (24 hour) PKC activation increases expression of intracellular and membrane-bound hERG protein. However, the increased channel abundance is not accompanied by an increase in hERG current (I_{hERG}). Our data reveal that acute (30 minute) PKC activation inhibits $I_{hERG,}$ and this effect is dependent on the N-terminus of the channel. Upon truncation of hERG's N-terminus, chronic activation of PKC increases both hERG protein expression and current. Our findings demonstrate that PKC activation regulates hERG in a balanced manner, altering both hERG current and expression. Funding: Natural Sciences and Engineering Research Council of Canada

26. **MOLECULAR MECHANISMS OF FENTANYL-MEDIATED SUDDEN DEATH.** Jared Tschirhart, Wentao Li, Jun Guo, Shawn Lamothe, and Shetuan Zhang**,** Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

Fentanyl use is associated with a high incidence of sudden death. Although fentanyl is known to induce respiratory depression, we wanted to determine if cardiac electrophysiology is also disrupted. The human ether a-go-go related gene (hERG) potassium channel is a common target for various compounds, including several prescription drugs. Drug blockage of the hERG channel prolongs cardiac repolarization, leading to arrhythmias and sudden death. Given the propensity of fentanyl to cause sudden death, we aimed to determine if fentanyl interferes with hERG. The effects of norfentanyl, a main metabolite, were also examined.
We used whole-cell voltage clamp to record potassium currents from human embryonic kidney cells stably expressing hERG. Fentanyl or norfentanyl were applied to the perfusion chamber during recordings to determine effects. First, a voltage protocol that mimics a cardiac action potential (AP) was used to elicit hERG currents. Our data reveal that fentanyl blocks hERG current with an IC_{50} of 0.27 μM, while norfentanyl does not block hERG. To determine the functional impact, we recorded APs in cardiomyocytes isolated from neonatal rats. Fentanyl (0.5 μM) significantly prolonged AP duration. The post-mortem blood concentration in fentanyl-overdose death ranges from 9 - 1140 nM. While our data are not sufficient to conclude that hERG block is exclusively responsible for fentanyl-related death, we provide a potential mechanism, especially for individuals whose cardiac electrophysiological functions are already compromised. Supported by the Canadian Institutes of Health Research, the Heart and Stroke Foundation of Canada, and the Natural Sciences and Engineering Research Council.

27. **ACUTE HYPERGLYCEMIA IMPAIRS ARTERY FUNCTION DURING THE LOW ESTROGEN, BUT NOT THE HIGH ESTROGEN, PHASE OF THE MENSTRUAL CYCLE.** JS Williams, T Stimpson, JC Tremblay, AM Fenuta, KE Pyke, School of Kinesiology and Health Studies, Queen's University, Kingston, Ontario.

Introduction. Acute hyperglycemia results in transient endothelial dysfunction in healthy males when assessed via endothelial-dependent flow-mediated dilation (FMD). However, research in female participants is lacking and the impact of menstrual phase (i.e. high estrogen [HE] vs. low estrogen [LE]) on vulnerability to acute hyperglycemia-induced endothelial dysfunction is unknown. It is hypothesized that hyperglycemia-induced endothelial dysfunction will be attenuated in the HE phase. **Methods**. Nineteen healthy, naturally menstruating women (age: 21 ± 1 years) were recruited for the study. Participant's endothelial function was tested via brachial artery FMD before and 60-, 90-, and 120-min after consuming an oral glucose challenge (75g glucose in solution) during their LE and HE phases. Blood samples were taken pre- and 30-min post-glucose ingestion for blood glucose (BG) and insulin (BI), and to assess sex hormone (estrogen, progesterone) levels. **Results**. BG and BI levels increased 30-min post-ingestion, with no difference between phases. Estrogen, but not progesterone, levels increased during the HE vs. LE phase. FMD was reduced during the LE phase at 90min post-ingestion by 27.6% ($p < 0.001$); however, FMD was not impaired during the HE phase. **Conclusion.** Acute hyperglycemia only resulted in endothelial dysfunction when estrogen levels were low. Cyclical elevations in estrogen during the menstrual cycle appear to offer protection against the impact of glucose in pre-menopausal women. Funding Sources: NSERC Discovery Grant & Canadian Graduate Scholarship – Master's

Health Policy, Population health, and Epidemiology

28. **THE RELATIONSHIP BETWEEN ESTABLISHED RISK FACTORS FOR COLORECTAL CANCER AND LINE-1 DNA METHYLATION**. Gogna P[1], King WD[1], [1]Department of Public Health Sciences, Queen's University.

Background: This research examines the association between established colorectal cancer risk factors and LINE-1 DNA methylation in health colon tissue, in order to investigate the role of LINE-1 DNA methylation as a mechanism by which established risk factors may lead to carcinogenesis. Materials and Methods: The study population consisted of 317 individuals undergoing colonoscopy screening. Multivariable linear regression was employed to examine associations of alcohol consumption, smoking, BMI, NSAID use, physical activity, and fruit and vegetable consumption with LINE-1 DNA methylation, while controlling for relevant confounders. Results: Alcohol consumption, smoking, BMI, NSAID use, physical activity, and fruit and vegetable consumption were not related to LINE-1 DNA methylation in this population. Discussion: This work presents novel investigations of relationships between NSAID use, and fruit and vegetable consumption with LINE-1 DNA methylation in the tissue of interest, and is an important addition to the sparse literature in this field.

29. **SCHOOL-BASED RELATIVE AGE EFFECTS IN CANADIAN ADOLESCENTS: A MENTAL HEALTH FOCUS.** Nathan King, MSc, Colleen Davison, PhD, William Pickett, PhD, Department of Public Health Sciences, Queen's University Kingston, Ontario Canada.

School-based relative age effects refer to the disadvantages incurred by the youngest students in the classroom. From an early age younger students are compared to their older peers who benefit from heightened maturity. When differences in maturity are mistaken for differences in innate ability, persistent relative age effects can develop. Previous research has identified that on average relatively younger students perform worse academically and experience more social difficulties. It has been hypothesized that differences stemming from relative age, including differences in participation and achievement can impact mental health. Younger relative age has been associated with an increased risk of internalizing symptoms, and youth suicide. However, the magnitude and extent of mental health disparities associated with relative age remains poorly understood. Epidemiological analyses will be conducted using data from the 2014 Health Behaviour in School-aged Children study (n≈ 30,000 Grade 6 to 10 students). Findings examining the associations between relative age and indicators of mental health in Canadian adolescents will be presented along with a conceptual model. Analyses will consider differences by demographic, family and school characteristics. Mental health issues are prevalent in adolescence and predictive of both short and long-term health and quality of life. Identifying ways of mitigating these effects is essential to ensuring all students have an equal opportunity to succeed, and live healthy and productive lives, irrespective of their date of birth.

30. **PSYCHOMETRIC ANALYSIS OF TWO NEW SCALES TO ASSESS TEACHERS' CONFIDENCE IN DELIVERING MENTAL HEALTH RELATED CONTENT IN THE CLASSROOM.** Brooke Linden, Dr. Heather Stuart**,** Public Health Sciences

The purpose of this study was to develop and psychometrically test two new scales to assess teachers' confidence in delivering mental health related content in the classroom. Our goals in this paper were (a) to outline the cognitive testing and content validation processes undertaken during the development and refinement of items, and (b) to assess the psychometric properties of the scales through exploratory factor analysis and internal consistency reliability analysis. Cognitive testing of both scales was conducted in a focus group setting with members of the Elementary Teachers' Federation of Ontario. Content validation was assessed through a Delphi method conducted among a sample of educational experts from an Ontario university. Data for the psychometric analysis was derived from the initial intake survey in the Let's Talk in the Classroom pilot project, an online teacher development tool designed to give elementary school teachers the tools and knowledge to develop lesson plans related to mental health. Exploratory factor analysis revealed two unidimensional scales. The Teacher's Confidence Scale contains 10 items measuring educators' confidence in delivering mental health related materials in the classroom. The What Worries Me Scale contains 10 items measuring concerns educators may have about discussing the topic of mental health in a classroom setting. Alpha coefficients for both scales suggested strong internal consistency reliability**. Supporting Agency:** Bell Canada (Bell Let's Talk)

31. **A RANDOMIZED-CONTROL TRIAL OF MULTI-PLATFORM AUDIOVISUAL TEACHING MODULES IN COLORECTAL SURGERY LEARNING PRESERVATION.** *Candy S, Mir ZM, Hanna N, Zevin B, &Patel SV.* Department of Surgery.

Innovative methods for curricular content delivery are constantly being developed, with new tools such as online modules taking the forefront. These tools are relatively new to surgical education and their utility and ability to act as a point of care review tool has not been well characterized. Our goal was to develop and evaluate audiovisual teaching modules for topics in anorectal diseases for use by medical students. Research ethics approval was obtained and a survey was created that combined knowledge based questions with a qualitative assessment of the videos. Forty-nine second-year medical students were recruited and randomized to either lecture alone or lecture and online audiovisual teaching modules (AV). All participants attended a lecture on anorectal diseases and then completed a pre-test survey. Participants in the AV group were then provided with access to the modules, subsequently, all students completed a post-test. The average pre-test score for the 49 participants was 9.7 $\pm$ 2.3 out of 18 questions. The post-test average for the AV group was 12.5 $\pm$ 1.6 compared to the lecture review alone group with 9.8 $\pm$ 2.0. The AV group showed a significant improvement on knowledge based questions when compared to the lecture group ($p<.0001$). This study demonstrates that audiovisual teaching modules can be highly effective teaching tools. As such similar modules could be useful across other General Surgery specialties.

32. **EMOTIONAL AND PHYSICAL CHILD ABUSE IN THE CONTEXT OF THE 2010 HAITI EARTHQUAKE.** Sony Subedi, Colleen Davison and Susan Bartels, Department of Public Health Sciences.

Objective: The aim of this study is to determine the household prevalence of emotional and physical abuse in children (aged 2-14) following the January 12, 2010 earthquake (7.0 Mw) that struck near Port-au-Prince, Haiti ii) and to explore the association between earthquake-related loss and experience of emotional and physical child abuse in the household. Methods: A nationally representative sample of Haitian households from the 2012 phase (n=13180) of the Demographic and Health Surveys (DHS) was used. Descriptive analysis was summarized using frequencies and measures of central tendency. The association between experiences of earthquake-related loss and emotional and physical child abuse was assessed using log-binomial regression models. Results: Approximately 77.0% of children aged 2-14 experienced at least one form of physical abuse and 78.5% of children experienced at least one form of emotional abuse one month prior to the 2012 survey period. Results regarding the second objective (association between earthquake-related loss and experiences of emotional and physical child abuse) are in process. Conclusions: The extremely high prevalence of emotional and physical child abuse in Haiti indicates an immediate need for improvements in the enforcement of existing policies and interventions aimed at decreasing child abuse in the household.

33. **A POPULATION BASED COHORT STUDY ON THE TRENDS OF CHILDHOOD INTUSSUSCEPTION IN ONTARIO.** Arany Theivendram[1], Mila Kolar[2], Michael McIsaac[1] and Susan Brogly[2]. [1]Department of Public Health Sciences and [2]Department of Surgery, Queen's University, Kingston, Ontario, Canada.

This study will explore various trends on childhood intussusception in Ontario through a population based cohort study from 1997 to 2016. Intussusception is the most common cause of intestinal obstruction in infants and young children. The treatment of this condition has evolved over the past 50 years from being uniformly surgical to predominantly non-operative management. Being part of a larger study on the trends and management of childhood intussusception, it is proposed that this study will assist in capturing pediatric intussusception in the Ontario population, which will then enable us to describe current practices and the magnitude of delayed diagnosis and complications. The main trends analyzed include trends by season and calendar year and its differences by age and sex. Other analyses include determining trends by calendar year in diagnostic and treatment approaches and determining the proportion of patients who were initially treated non-surgically, who had failure of nonsurgical management and were treated surgically, by hospitalization centre. This study will allow us to see current practices and outcomes and compare them to other developed countries, in order to then define areas for both improvement and better utilization of resources. Supported by Queen's Department of Surgery.

Inflammation, infection and immunity

34. **EVALUATING CYTOKINE PRODUCTION BY DIFFERENT MACROPHAGE SUBSETS IN RESPONSE TO VIRUS INFECTION.** Torki Alothaimeen[1], Sam Basta[1] and Katrina Gee[1]. [1]Department of Biomedical & Molecular Science Queen's University, Kingston, Ontario, Canada.

Granulocyte-macrophage colony-stimulating factor (GM-CSF) and Macrophage colony-stimulating factor (M-CSF) can modulate differentiation and functions of macrophages (MΦ). Bone marrow derived macrophages (BMDMs) that were cultured in GM-CSF or M-CSF are termed GM-CSF MΦ or M-CSF MΦ, respectively. Recent studies showed that GM-CSF MΦ are more likely to produce more pro-inflammatory cytokines following LPS treatment than M-CSF MΦ. Currently, how these two types of MΦ respond to viral infection is unknown. To investigate this issue, we infected both cell types with 2 related strains of Lymphocytic Choriomeningitis Virus (LCMV) - LCMV-Cl 13 or LCMV-ARM and then measured several cytokine responses *in vitro*. GM-CSF infected cells preferentially produced IL-6, whereas, conversely, M-CSF infected cells generated more IL-10. GM-CSF could not produce detectable IL-12p70 or IL-23 after infection. Following LCMV, GM-CSF cells were able to induce more IL-6 by ARM comparing to Cl 13, whereas M-CSF infected with ARM produced more IL-10 than Cl 13. Thus, GM-CSF and M-CSF demonstrate, at the level of cytokine production, different immune responses with implications for their respective roles in viral infection.

35. **TEMPORAL ANALYSIS OF CHRONIC SPINAL CORD INJURY PAIN.** Courtney Bannerman[1], Julia Segal[1], Jaqueline Silva[1], Scott Duggan[2], Nader Ghasemlou[1,2] [1]Department of Biomedical and Molecular Sciences, [2]Department of Anesthesiology.

Translating research from laboratory animal studies to human applicability is one of the more challenging steps in biomedical research. In the case of a human spinal cord injury (SCI), there is sustained pressure on the spinal cord after the injury until it can be surgically relieved. The current rodent model does not accurately reflect the injury sustained by humans. From this study we aim to characterize a more clinically relevant model of spinal cord injury: the compression injury. The contusion surgery is performed on female C57BL/6J mice that are at least 8 weeks of age. A contusion and compression contusion are performed with the Infinite Horizons impactor device. The procedure for the sham (control) mice is completed in a similar manner minus the impact. Over a period of 6 weeks post-injury, the mice are scored for mechanical, thermal cold, and thermal heat sensitivity using the Von Frey assay, the acetone test, and the Hargreaves radiant heat test, respectively. The locomotor recovery is assessed using the Basso Mouse Scale (BMS). The mice who received the compression injury show significantly greater thermal heat and mechanical hypersensitivity in comparison to a contusion injury as well as significantly lower BMS scores. Creating a rodent model of spinal cord injury that more closely mimics an injury sustained by humans helps facilitate the translation of potential therapeutics from mouse to human.

36. **THE MICROBIOME: A NOVEL MODULATOR OF THE FVIII IMMUNE RESPONSE.** Tarrant J, Cormier M, Nesbitt K, Dwyer C, Hough C, and David Lillicrap. Department of Pathology and Molecular Medicine, Queen's University Kingston, Ontario Canada.

Hemophilia A (HA) is an inherited disease, characterized by a mutation in the Factor (F)VIII gene resulting in low circulating levels of FVIII protein. It is the most common severe bleeding disorder, and if untreated, results in spontaneous prolonged joint bleeds and debilitating arthritis. Intravenous replacement of FVIII protein is the gold-standard treatment but neutralizing IgG antibodies against FVIII are generated in up to 30% of patients, rendering it ineffective. Most known risk factors are non-modifiable and do not explain all incidences of antibodies. We propose that the gastrointestinal microbiome is a novel risk factor. This complex community of microorganisms residing primarily in the colon is a key factor in the pathogenesis of many immune-mediated diseases. We have demonstrated that FVIII treated HA mice with disrupted gut microbiomes (following antibiotic treatment) generated significantly more anti-FVIII IgM antibodies compared to untreated controls ($p<0.0001$). DNA sequencing of cecal contents revealed that the antibiotic treatment reduced relative abundances of the *Lactobacillus* and *Clostridia* which are known to produce immunosuppressive metabolites. Additionally, our HA germ free mouse model showed a significant reduction in the incidences of anti-FVIII IgG production after FVIII administration compared to regular controls ($p<0.001$). This data indicates that the gut microbiome is involved in the FVIII antibody response and provides a rationale to further investigate therapeutic methods to reduce FVIII-neutralizing antibodies in HA patients. (Supported by the Canadian Hemophilia Society and the Canadian Institutes of Health Research

37. **IL-27 AMPLIFIES CYTOKINE RESPONSES TO GRAM-NEGATIVE BACTERIAL PRODUCTS AND SALMONELLA TYPHIMURIUM INFECTION**. Carlene Petes1, Natalya Odoardi1, Samantha M. Plater1, Nancy L. Martin1, Katrina Gee1,1 Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

Cytokine responses from monocytes and macrophages exposed to bacteria are of particular importance in innate immunity. Focusing on the impact of the immunoregulatory cytokine interleukin (IL)-27 on control of innate immune system responses, we examined human immune responses to bacterial products and bacterial infection by *E. coli* and *S. typhimurium*. Since the effect of IL-27 treatment in human myeloid cells infected with bacteria is understudied, we treated human monocytes and macrophages with IL-27 and either LPS, flagellin, or bacteria, to investigate the effect on inflammatory signaling and cytokine responses. We determined that simultaneous stimulation with IL-27 and LPS derived from *E. coli* or *S. typhimurium* resulted in enhanced IL-12p40, TNF-α, and IL-6 expression compared to that by LPS alone. To elucidate if IL-27 manipulated the cellular response to infection with bacteria, we infected IL-27 treated human macrophages with *S. typhimurium*. While IL-27 did not affect susceptibility to *S. typhimurium* infection or *S. typhimurium*-induced cell death, IL-27 significantly enhanced proinflammatory cytokine production in infected cells. Taken together, we highlight a role for IL-27 in modulating innate immune responses to bacterial infection. Research supported by Natural Sciences and Engineering Research Council (NSERC). CP is supported by NSERC PGS-D.

38. **INVESTIGATING THE SIGNALING PATHWAYS OF MURINE MACROPHAGES AFTER STIMULATION OF TLR-7 WITH SSRNA ANALOGUES AND VIRUS INFECTION.** Evan Trus[1], Torki Alothaimeen[1], Katrina Gee[1], Sam Basta[1], [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada.

Lymphocytic Choriomeningitis Virus (LCMV) is a segmented, single stranded RNA virus belonging to the *arenavirus* family. Capable of infecting many different types of mammalian cells, LCMV has been commonly used as a model for both chronic and acute viral infections, contributing to the understanding of various aspects of the immune system. A key defense against LCMV infection is the macrophage. Little work has been done to directly evaluate the relationship of LCMV and macrophages, especially with regards to LCMV infection of macrophages. However, previous research has shown that macrophages have an essential role in the early control of LCMV infection and that infection induces transient inflammatory monocytosis after acute infection mediated by TLR 7. TLR7, an endosomal pattern recognition receptor specific for ssRNA and has been shown to be required for clearance of certain LCMV strains. In this study we seek to determine the effects that infection with LCMV has on both main macrophage types, M1 and M2. We found that LCMV suppresses the activation of the TLR7 signaling pathway while promoting the production of proinflammatory cytokines in M1- and M2-like macrophages respectively. This study provides insights into the differing reactions M1- and M2-like macrophages have upon LCMV infection, potentially having wider implications on the understanding of arenavirus pathogenesis. Additionally, the insights from this study will inform future inquiries into viral mechanisms of innate immune interference, particularly with regards to TLR7. Research supported by Natural Sciences and Engineering Research Council (NSERC). ET is supported by DBMS/NSERC.

Neuroscience Research

39. **CHARACTERIZING RESPONSE INHIBITION DEFICITS IN ADOLESCENTS SHOWING EARLY SIGNS OF BORDERLINE PERSONALITY DISORDER USING AN OCULOMOTOR TASK.** O. G. CALANCIE[1], A. C. PARR[1], L. BOOIJ[2], D. BRIEN[1], B. C. COE[1], S. KHALID-KHAN[1], D. P. MUNOZ[1], [1]Centre for Neuroscience Studies, [2]Psychology, Queen's Univ., Kingston, ON, Canada

Adults with Borderline Personality Disorder (BPD) - a severe psychiatric illness that begins in adolescence - show impaired saccadic control in response inhibition tasks. To test whether this pattern also exists in adolescents showing early signs of BPD, we measured saccade performance in female adolescents with BPD traits and age-matched female controls while they performed an interleaved pro- and anti-saccade task. Participants generated anti-saccades (voluntary saccade away from salient target) or pro-saccades (automatic saccade toward target) depending upon a color instruction. BPD adolescents generated more anticipatory saccades (saccade reaction time (SRT): <90 ms) on anti-saccade trials compared to controls, indicating dysfunction of saccadic preparatory suppression signals within the oculomotor network. Direction errors, express saccades (SRT: 91-139 ms), and regular latency saccades (SRT: >140 ms) did not differ between groups, suggesting intact functioning of visually-guided oculomotor signaling in BPD patients. Similar behavior is depicted in adults with BPD, suggesting that inhibitory dysfunction - specifically a failure to adequately *prepare* for an inhibitory command - develops early in disease progression. This result is distinct from other psychiatric disorders characterized by impulsivity in youth (i.e., ADHD) where dysfunction is evident by increased prevalence of direction errors during the propagation of express and regular latency saccades. We hypothesize that impulsivity across youth clinical disorders may correspond to distinct impaired signaling circuits within the frontostriatal regions of the oculomotor network. ***Supporting Agency:*** This work was supported by a research operating grant from SEAMO Innovation Fund (project #365350) to OGC, DPM, LB and SKK.

40. **MEMORY LABILITY, RETRIEVAL PRACTICE & LONG-TERM MEMORY IN A HUMAN GROSS ANATOMY COURSE**. Joshua C. Goheen, Ronald A. Easteal, Mohammad B. Azzam, Rylan G. Egan and Carolyn J. Perry. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON K7L 3N6, Canada.

It has been demonstrated that test-enhanced learning in the form of retrieval practice (RP) is more effective than repeated study alone. Current RP studies normally do not take full advantage of the lability of memories during retrieval. The following study combined multiple forms of RP in attempt to maximize learning and retention through the manipulation of information during labile phases. Students in a large, third-year anatomy class were asked to review content pertaining to the upcoming lecture/lab prior to sleep. Students underwent RP preceding a congruent lecture or lab period. Questions where structured to bridge prior knowledge to the upcoming lecture material in hope to grow a labile memory and enhance learning. Students were tested using the online platform TopHat™ in both lecture (LRP) and in lab (LABRP). Students were given course credit as an incentive to participate in the study and this participation was monitored. Over 200 questions across both LRP and LABRP were posed to the students. Preliminary analysis indicates that the amount of retrieval conducted on concepts in individual exam questions is proportional to the amount of correct responses on those questions.

41. **IDENTIFICATION OF CO-EXPRESSION NETWORK ASSOCIATED WITH CHRONIC PAIN IN SPINAL CORD INJURY PATIENTS.** Suleman Gul Khan[1], Margot Gunning[1], Jihoon Choi[1], Courtney Bannerman[1], Nader Ghasemlou[1], Qingling Duan[1,2], [1] Department of Biomedical and Molecular Sciences, Queen's University, [2] School of Computing, Queen's University.

Background: Spinal cord injury (SCI) is known to affect nearly 33,000 citizens in Ontario to date. Treatment options for patients with chronic pain post SCI are often ineffective and can also carry high risk of abuse and societal burden. The aim of this study is to identify functional biological pathways and mechanisms underlying chronic pain in SCI patients using various machine learning approaches. **Methods:** We obtained microarray gene expression data extracted from peripheral blood mononuclear cells (PBMCs) of 25 patients with SCI using the Gene Expression Omnibus (GEO) database. Study population was divided into two groups: 12 patients with chronic pain (case cohort) and 13 patients without pain (control cohort). Using the microarray gene-expression data we grouped genes into co-expression modules based on similarity. By applying the Weighted Gene Co-expression Network Analysis (WGCNA) we executed an unbiased approach in our data analysis and network construction. **Results:** Gene set enrichment analysis (GSEA) and protein functional pathway analysis was used to identify regulatory classes of genes that are over represented within our network. We identified networks of co-expressed genes that are correlated with chronic pain phenotype in our SCI patients. **Conclusions:** We have identified groups of co-expressed genes that are associated with pain signal in SCI patients. Findings from this study could potentially be used in the discovery of novel drug targets, which we aim to further validate using animal models. Furthermore, these findings will allow us to enhance our understanding of the biological pathways and mechanisms involved in chronic pain. Project financially supported by: Conquer Paralysis Now and The Bryon Riesch Paralysis Foundation

42. **POPULATION DYNAMICS IN A RODENT MODEL OF FOCAL ISCHEMIC STROKE: BARRIER TO PRE-CLINICAL THERAPEUTIC TRANSLATION?** Kathleen A. Harrison & Douglas J. Cook. Centre for Neuroscience Studies, Queen's University Kingston, Ontario Canada.

Lack of treatment options has resulted in stroke being the leading cause of adult disability in Canada. Despite thousands of investigations, no new therapies have been produced. Though controversial, limited preclinical success of compounds may be related to flaws in experimental disease modelling via rodent models. Specifically, variation in ischmic lesion volume following middle cerebral artery occlusion (MCAO) can confound efficacy evaluation. To elucidate lesion volume variability following a surgical model of stroke, 165 Sprague Dawley rats underwent MCAO. Perfusion deficit was inferred by behavioural evaluation during ischemic induction. 150 animals were evaluated at 24hours post-ischemic injury, gross lesion volume was evaluated by Tetrazolium Chloride histological staining at 24 hours. Stroke volumes were calculated through a semi-automated image analysis pipeline. Stroke volumes averaged ~9.8% ± 8.4% (Min = 0%; Max = 32.3%). Though 80% of animals had indication of cerebral infarction, only 52% of lesions involved neocortex. Correlations were found between 24 hour volume and 24 hour behavioural deficits, but acute behavioural deficit did not predict lesion volume. Thus, these results confirm other published values regarding high population variance following MCAO in Sprague Dawley linage. Animal models are to help in elucidating treatment of human disease. Current methods of MCAO modelling may be insufficient for pre-clinical investigations, as high variability can easily result in a false positive effects of neuroprotective treatments.

43. **MORPHOMETRIC ANALYSIS OF DORSAL HIPPOCAMPAL NEURONS IN A MOUSE MODEL OF SPORADIC ALZHEIMER'S DISEASE**. Rasha H. Mehder, Brian M. Bennett, R. David Andrew, Department and Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

The study of late-onset (sporadic) Alzheimer`s Disease (LOAD) has been hindered by the lack of animal models. Oxidative stress is a causative factor in LOAD, and we have developed an oxidative stress-based model of age-related cognitive impairment based on gene deletion of aldehyde dehydrogenase 2 (Aldh2), an enzyme important for the detoxification of endogenous aldehydes arising from lipid peroxidation. These mice exhibit a progressive decline in recognition and spatial memory, decreased hippocampal volume, and a number of AD-like pathological changes. In the current study, we performed morphometric analyses in the hippocampal CA1 region to determine whether altered neuronal structure might account for the observed cognitive impairment and hippocampal volume loss. Dendritic morphology of one year old mice was quantitatively analyzed following Golgi-Cox staining using 9 wildtype (WT) mice (37 neurons) and 15 Aldh2 null mice (60 neurons). Four to 6 pyramidal neurons were traced per mouse, followed by branched structured analysis and Sholl analysis of dorsal hippocampal CA1 pyramidal neurons. Our evaluation of neuronal morphology and complexity of neurons from Aldh2 null mice showed significant reductions in apical and basal dendritic length, and a reduction in the number of dendrite intersections, ends, and nodes, compared to WT controls. These findings indicate that CA1 dendritic complexity is significantly reduced in Aldh2 null mice, and suggest a structural basis for the cognitive deficits and reduced hippocampal volume seen in this LOAD model.

44. **RETRIEVAL PRACTICE FOR LEARNING LEADING TO BETTER LONG-TERM RETENTION AND IMPROVED STUDENT PERFORMANCE**. Mohammad B. Azzam, Ronald A. Easteal, Joshua C. Goheen, and Rylan G. Egan. Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON K7L 3N6, Canada.

Learning is thought to occur only during episodes of repeated studying (reading and memorization). The literature demonstrates, however, that retrieval practice (RP) is a better tool at enhancing learning and long-term retention, when compared to studying alone. The current study investigated the significance of RP on student performance on both theoretical (multiple-choice questions; MCQs) and lab practical (bell-ringer) evaluations in a large third-year gross anatomy course. It was hypothesized that students who participated (experimental group) in RP performed better than students who did not (control group). All specimens used in the current study were obtained from the Anatomy Learning Centre at Queen's University. Participants were awarded a scaled participation grade for lecture RP, while participation in lab RP was completely voluntary. In lectures, participants answered MCQs using the online platform Top Hat^{TM}; during weekly lab sessions, participants answered bell-ringer-style questions. All correct answers (feedback) were given. In addition, in week 6, the participants completed a mock bell-ringer of 60 questions. The final theoretical and practical grades of the experimental and control groups were analyzed and compared. Preliminary analyses indicated that the students' performance was enhanced when RP was implemented. It was concluded that RP was more effective than repeated studying alone, in enhancing the learning of, and therefore, the long-term retention of, course material.

45. **AROMATASE EXPRESSION IN THE NEOCORTEX OF ADULT MALE RATS.** Chloe N. Soutar[1] , Patrick Grenier[2] , Mary C. Olmstead[1, 2], and Hans C. Dringenberg[1, 2] , [1]Centre for Neuroscience Studies, Queen's University, Kingston, ON, [2]Department of Psychology, Queen's University, Kingston, ON

The steroid hormone 17β-estradiol (E2) rapidly influences synaptic activity and plasticity in the rodent forebrain. Expression of aromatase, the enzyme responsible for the synthesis of estrogens from androgen precursors, has been well described in the sensory neocortex of primates and mice and in the hippocampus and subcortical regions of rats. To date, there are no reports of aromatase expression in the neocortex of adult rats. Thus, we examined the expression pattern and cellular localization of aromatase in the neocortex of adult male rats using 3,3'-diaminobenzedine immunohistochemistry (DAB IHC) and immunofluorescence. Preliminary data reveal that aromatase is expressed throughout the medial prefrontal cortex (mPFC), primary somatosensory cortex (S1), primary auditory cortex (A1), and primary visual cortex (V1). In all regions, aromatase immunoreactivity appears to be restricted to the perikarion. Colocalization studies show that aromatase is expressed by neurons across cortical layers II-VI. DAB IHC data show that, in A1, the number of aromatase-expressing cells increases linearly across cortical layers and does not differ significantly between hemispheres. Preliminary data suggest a similar pattern of aromatase expression in V1. These findings indicate that the adult rat neocortex is highly enriched with aromatase and is, thus, a site of E2 synthesis. Ongoing experiments center on examining the colocalization of cortical aromatase with markers for glia and glutamatergic cells. Supported by NSERC and CIHR.

46. **INDUCED CELL-MEDIATED DELIVERY OF GLIAL CELL LINE DERIVED NEUROTROPHIC FACTOR IS NEUROPROTECTIVE FOR MYENTERIC NEURONS**. Demetri P. Zoumboulakis, Sandra Lourenssen, Jacob Pyche, Michael Blennerhassett, Department of Medicine, GIDRU, KGH

Transmural inflammation of the intestine causes structural and functional alteration of the enteric nervous system (ENS), that contributes to dysmotility. Elsewhere, neurotrophins can promote survival and recovery from damage, but a similar role for glial cell line derived neurotrophic factor (GDNF), the principal neurotrophin for the ENS, is poorly understood. This was investigated in an intestinal neuromuscular co-culture model, consisting of myenteric neurons, smooth muscle and glia. Human embryonic kidney (HEK) cells were transfected with a GDNF-GFP adeno-associated virus plasmid as a cell-mediated source of GDNF, and combined with neurons in models of ischemia, inflammatory damage and structural damage. Mechanical axotomy typically caused a 53±3% loss of enteric neurons by 48 hr, but addition of GDNF-GFP transfected HEK cells prevented this entirely ($p>0.05$ vs control). The NO-donors SNP (200 μM) and DETA-NONO (300 μM) caused selective loss of 43±8% and 57±5% of neurons respectively, but addition of GDNF-GFP HEK cells prevented this ($n=4$-5). Metabolic inhibition (DNP; 0.75 mM) reduced neuron number by 51±7%, which was prevented by GDNF-GFP HEK cell addition. These effects were similar to exogenous GDNF (50 ng/mL). We conclude that a cell-mediated source of GDNF is highly effective in preventing neuronal loss or damage in vitro. This suggests that a similar approach in vivo that uses induced expression of GDNF may support the ENS in diverse disease conditions. Supporting Agency: NSERC

Patient Care and Nursing Research

47. **SPEAC (SAMPLING PATIENT EXPERIENCE TO ASSESS COMMUNICATION): A PILOT IMPLEMENTATION STUDY IN CLINICAL CLERKSHIP.** Sachin Pasricha[1], Juliana Sunavsky[1], Adam Mosa[1], MSc, Eleni Katsoulas[2], MEd, Andrea Winthrop[2,3], MD, FRCS(C), [1]School of Medicine, Queen's University, [2]Undergraduate Medical Education Program, Queen's University, [3]Department of Surgery, Queen's University.

Background: Communication is essential to assess in medical students in the clinical learning environment. Currently, workplace-based assessment relies primarily on preceptor feedback. A previous needs assessment identified support from patients, students and faculty for soliciting patient feedback on students' communication skills. We report here our implementation pilot of patient feedback and evaluation of its utility and feasibility. **Methods:** Using a feedback tool with a published validity argument, students solicited feedback from patients in inpatient settings while clinic staff solicited feedback in ambulatory clinics. The pilot was evaluated via interviews and questionnaires. **Results:** 114 patients, 23 students, 6 faculty, and 16 clinic staff participated. During the study, 111 patients provided feedback in clinics, compared with 3 in inpatient settings. Using qualitative analysis of the evaluation questionnaires and interviews, we identified 75 patterns and 8 themes. Feasibility barriers to self-soliciting patient feedback in inpatient settings included low patient turnover, fast-paced environment, feedback tool length, and patient vulnerability. Students and faculty felt that patient feedback is valuable, and that open-ended questions could lead to more constructive feedback. **Conclusion:** Obtaining patient feedback on students' communication skills is useful and feasible when solicited by a third party in ambulatory clinics. This source of assessment data should be considered for integration into a competency based system of assessment in the clinical clerkship.

48. **CONCEPT ANALYSIS OF BODILY INTEGRITY IN INFANTS BORN INTERSEX/WITH DISORDERS OF SEX DEVELOPMENT.** Jennifer Carroll, BScN, RN, Master of Nursing Science Student, Queen's University, Rosemary Wilson, RN(EC), PhD, Associate Professor, School of Nursing, Queen's University.

Bodily integrity is central to discussions of intersex/disorders of sex development (DSD). For infants born with ambiguous external genitalia immediate and long-term treatment choices must be made affecting the child's bodily integrity. This poster presents an analysis of bodily integrity as it pertains to infants born with DSD/intersex using Walker and Avant's (2011) method of concept analysis. Philosophically, bodily integrity is grounded in the idea of the body as something which both connects and separates the self from the world. These discussions inform the medical-legal and medical-ethical literature wherein bodily integrity is an integral facet of personal autonomy the violation of which requires consent. Social science and social justice literature describe bodily integrity as a central feature of one's autonomy that must be protected. Congruity, autonomy, transformation, and temporality are the defining attributes of bodily integrity. The antecedents and consequences for each of these attributes are elucidated. Model, contrary, borderline, related, and illegitimate cases presented connect the abstract concept and its components to the lived reality. Bodily integrity in the context of infants born intersex/with DSD can be delimited by: the congruity of the external, physical self and the internal embodiment of self; the social relation of self with others yet individuated from them; the transformation of self in response to new experience; experience (or potential for experience) over time.

Protein Structure and Function

49. **REGIONS CONNECTING THE MEMBRANE SPANNING AND NUCLEOTIDE BINDING DOMAINS OF MULTIDRUG RESISTANCE PROTEIN 1 (MRP1) ARE FUNCTIONALLY DISTINCT.** Emma E. Smith, Gwenaëlle Conseil and Susan P. C. Cole, Department of Pathology and Molecular Medicine.

The MRP1/ABCC1 transporter confers multidrug resistance by reducing intracellular drug accumulation through active efflux across the plasma membrane. MRP1 also effluxes xeno- and endobiotic organic anions that include estradiol glucuronide ($E_2$17βG) and leukotriene C_4 (LTC_4). MRP1 has three membrane spanning domains (MSD) that form the solute translocation pathway, and two nucleotide binding domains (NBD) which bind and hydrolyse ATP. MSD1/2 are linked to NBD1/2 by connecting regions (CR) 1 (aa 600-642) and CR2 (aa 1249-1291), respectively. To test the hypothesis that the CRs have distinct roles in MRP1 structure and function, Ala substitutions of eight conserved CR1 and CR2 residues were generated. Cellular levels of three of four CR1 mutants (S612A, R615A, E624A) were lower than wild-type MRP1 (by 60%, 95%, 95%, respectively; $p<0.05$). Of the four CR2 mutants, only W1287A cellular levels were markedly reduced (by 80%; $p<0.05$). A bovine Mrp1 cryo-EM structure suggests that some mutation-sensitive residues may participate in stabilizing interactions. This idea was not supported by the characterization of double exchange mutants, which failed to restore MRP1 levels. For CR mutants expressed at levels similar to wild-type MRP1, only CR2-G1291A exhibited a substrate-selective change in [^{3}H]LTC_4 transport (reduced by 40%; $p<0.05$) whereas [^{3}H]$E_2$17βG transport was unaffected. Our results suggest that CR1 is more important than CR2 for stable MRP1 expression, whereas CR2 may play a larger role in MRP1 function. Supported by CIHR grant MOP-133584

50. **PERCEIVED DISTANCE TO SPECIALIST MEDICAL CARE AND OBSTRUCTIVE SLEEP APNEA DIAGNOSIS IN RURAL SASKATCHEWAN.** Catherine Spagnuolo[1], Michael McIsaac[1], James Dosman[2], Chandima Karunanayake[2], Punam Pahwa[2] and William Pickett[1], [1]Department of Public Health Sciences, Queen's University, [2]Canadian Centre for Health and Safety in Agriculture, University of Saskatchewan.

Purpose: This study aimed to: (1) determine whether the proportion of adults with suspected undiagnosed obstructive sleep apnea (OSA) in rural populations varied by perceived distance to specialist medical care; and (2) assess whether any patterns observed were attributable to differences in the frequency of diagnosis among adults who would require specialist medical services related to sleep-disordered breathing. **Methods:** We used a cross-sectional epidemiologic study design, with longitudinal confirmation of key findings. Our study base included adults who completed the 2009 baseline questionnaire for the Saskatchewan Rural Health Study; longitudinal follow-up occurred until 2015. 6525 adults from 3731 households made up our sample. Statistical analysis used log-binomial regression. **Findings:** Rural adults who perceived the farthest distances (≥ 250 km) to specialist medical care were 1.17 (95% CI: 1.07, 1.29) times more likely to have suspected undiagnosed OSA compared to those who perceived the closest (< 100 km; referent) distances. However, there was no reported difference across distance quartiles in the frequency of sleep apnea diagnosis among adults who, based on their reported symptoms, possibly required specialist medical services related to sleep-disordered breathing. **Conclusions:** Perceived accessibility barriers are one possible risk factor for inadequate diagnosis and treatment of OSA. In rural Saskatchewan, there was an increased proportion of suspected undiagnosed OSA with increasing perceived remoteness from specialist medical care. Given the serious implications of undiagnosed and untreated OSA on the health of people and populations, increasing awareness of sleep apnea and existing sleep specialist services to improve individual perceptions about such care and its importance, as well as improving access to screening, diagnostic and treatment services for OSA would likely be impactful in rural and remote communities. (Supported by the Canadian Institutes of Health Research Frederick Banting and Charles Best Canada Graduate Scholarships Master's (CGS-M) program)

51. **THE ROLE OF THE *FUSARIUM GRAMINEARUM* STE2P RECEPTOR IN THE PATHOGENIC INFECTION OF WHEAT.** Pooja Sridhar[1], Daria Trofimova[1], John Allingham[1], Michele Loewen[1,2], [1]Queen's University, Department of Biomedical and Molecular Sciences, Kingston, Canada.[2]National Research Council of Canada, Ottawa, Canada.

Fusarium graminearum, a fungal pathogen of cereal crops, causes Fusarium Head Blight (FHB) in wheat, leading to decreased grain quality and deposition of harmful mycotoxins. It is currently unknown what directs the growth of *F. graminearum* to enable wheat cell penetration and infection. Recent research on a related *Fusarium oxysporum* species demonstrated that its directed growth, or chemotropism, towards its host was mediated by Ste2p, a pheromone sensing receptor in fungi. The Ste2p-mediated chemotropism was shown to be in response to the catalytic activity of a plant-secreted peroxidase. Our study investigates whether this mechanism of initiation of infection is conserved in *F. graminearum*, and more broadly across other fungal species. We found that *F. graminearum* exhibits positive chemotropism towards certain stimulants, which is eliminated upon knocking out the Ste2p receptor. FgΔ*ste2* also exhibits hyphal defects and reduced conidiation and will be assessed for its pathogenicity on wheat. RNA-seq and quantitative PCR will be performed to identify and validate the signaling pathway activated. In the longer term, the specific product of plant-secreted peroxidase will be identified by testing potential substrates of the plant peroxidase. Understanding the mechanism of chemotropism should reveal new targets for development in the defense of wheat from this pathogen. This project is funded by the National Research Council of Canada and Natural Sciences and Engineering Research Council of Canada.

52. **ENGINEERING A MULTI-FUNCTIONAL CAZYME COMPLEX WITH ENHANCED AGAROSE-DEGRADING PROPERTIES.** Keegan B. Turner-Wood, Julie Grondin, Benjamin Pluvinage, Alisdair B. Boraston, Holly L. Spencer, Steve Smith, Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada. (Supported by NSERC)

As the need for renewable energy sources becomes an ever-pressing matter, the search for new repositories has led researchers to explore the heretofore untapped option of plant cell polysaccharides. Representing the most abundant organic molecules on the planet makes them a very appealing target for generating biofuels and high value commodities. Despite the difficulties associated with digesting recalcitrant carbohydrate matrices, such a vast energy source has proven too attractive to microbial organisms, which have evolved biological nanomachines to digest and uptake this extensive carbon repository. Specialized carbohydrate active enzymes (CAZymes), which efficiently digest polysaccharides, have evolved in bacteria and fungi, allowing them to subsist from the insoluble carbohydrates found in their environment. Further advancements have evolved within certain saccharolytic microbes by way of extracellular molecular scaffolds termed cellulosomes, onto which CAZymes are anchored via species-specific protein binding. The association of CAZymes to a molecular scaffold greatly enhances their catalytic ability by increasing synergistic digestion via proximity and targeting effects. We propose to design a chimeric scaffold and attach enzymatic subunits with different carbohydrate specificities to alter the complex's target from cellulose to agarose. By harnessing the power of the cellulosome we aim to open the door to generating industrial quantities of secondary bio-fuels and other high value chemicals. A chimeric agarosome has been designed, which will bear *Bacteroides uniformis* sourced agarases.

Rehabilitation Science

53. **HEALTH SCIENCES RESEARCH USING ONLINE METHODS: CONSIDERATIONS FOR NOVICE RESEARCHERS.** Shikha Gupta and Atul Jaiswal, PhD Candidates, School of Rehabilitation Therapy, Queen's University.

The role of internet in the landscape of health sciences research has been expanding. The increasing internet penetration has provided an immense opportunity for the researchers to surpass geographical divide, build a global research community, and use technological advancements for research implementation and dissemination. While these online methods provide an opportunity to the researchers, their use also brings considerable ethical and legal concerns, especially while collecting sensitive health information. Therefore, young researchers who intend to employ online research methods in their projects, it is imperative to know what is online or internet-based research, how it is conceptualized and what are the key ethical concerns to consider while employing different types of online research methods. Focusing on the Canadian context, we present some of the points of dispute from ongoing scholarly debate, highlighting grey areas where uniform guidelines are lacking. Overall, it has been suggested that each type of online research methods (i.e. observational, interactive, or survey/interview research) is highly contextual and involve different levels of engagement and interaction between the participant and the researcher, which has an implication for ethics. Keeping participants' expectations, perceptions, and awareness about privacy is one of the key elements. With the careful design, planning, and implementation, researchers can deal most of these challenges efficiently while ensuring that the participants' privacy rights are protected and standards for ethical practices are met.

Reproduction and Sexual Function

54. **EFFECTS OF CARBON MONOXIDE ON VASCULAR ADAPTATIONS DURING PREGNANCY.** Megan Dickson[1], Karalyn McRae[1], Nichole Peterson[1], Graeme Smith[1,2]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, [2]Department of Obstetrics and Gynaecology, Queen's University, Kingston, Ontario

Introduction: Preeclampsia (PE) is characterized by abnormal placentation and systemic vascular dysfunction. Carbon monoxide (CO) is actively being studied as a potential therapeutic for PE due to its vasodilatory, angiogenic, and anti-inflammatory properties. CO has been shown to increase uteroplacental vascular growth in mice, however it is unclear through what mechanisms CO may be acting. Here, we aim to determine the effects of CO on markers of angiogenesis and inflammation at the maternal fetal interface and systemically during pregnancy. **Methods:** CD-1 mice were administered 250 ppm CO, or ambient air, on gestational day (GD) 0.5 until sacrifice at GD10.5 or GD16.5 (n=5/treatment/time-point). A quantitative real-time PCR array was used to determine expression of angiogenic and inflammatory related genes at the maternal fetal interface. Systemic markers were analyzed throughout gestation (GD0.5, 5.5, 10.5, 16.5) using a cytokine multiplex plasma assay. Data were analyzed using the $\Delta\Delta$Ct method and two-way ANOVAs, respectively. **Results:** On GD10.5, genes encoding VEGF and angiopoietin receptors, eNOS, and cell adhesion molecules were upregulated in CO treated mice. No changes were observed on GD16.5 ($p>0.05$). CO treatment had no effect on systemic cytokine levels ($p>0.05$). **Conclusion:** These results provide evidence that CO upregulates genes in major angiogenic pathways at the maternal fetal interface mid-gestation. Understanding how CO modulates angiogenesis during pregnancy is crucial prior to therapeutic use. (Supported by CIHR)

55. **THE NOVEL POST-ACTIVATION INVOLVEMENT OF POST-ACROSOMAL SHEATH RESIDENT GLUTATHIONE-S-TRANSFERASE OMEGA 2(GSTO2) IN NUCLEAR DECONDENSATION AND MALE PRONUCLEAR FORMATION.** Hamilton, Lauren E.[1], Suzuki, Joao[2], Mao, Jiude[3], Mienhson, Marie Charlotte[2], Xu, Wei[1], Sutovsky, Peter[3,4], and Richard Oko[1]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, [2]Department of Veterinary Sciences, Center for Research in Reproduction and Fertility, Universite de Montreal, St. Hyacinthe, QC, Canada, [3]Division of Animal Sciences, College of Food, Agriculture and Natural Resources, and [4]Department of Obstetrics, Gynecology and Women's Health, School of Medicine, University of Missouri, Columbia, Missouri, USA

The post-acrosomal sheath (PAS) of the perinuclear theca (PT) is the first compartment of the sperm head released into the ooplasm upon sperm-oocyte fusion, implicating its constituents in early zygotic developmental events. This study investigates the role of GSTO2, an oxidative-reductive enzyme found in the PAS- and perforatorial- PT of the sperm head and the ooplasm. GSTO2 conjugates glutathione, an electron donor previously implicated in nuclear decondensation and pronuclear formation, to make and break disulfide bonds. We hypothesize that sperm-borne GSTO2 enzymes participate in nuclear decondensation initiation and pronuclear formation before the recruitment of GSTO enzymes from the ooplasm. Through inhibition studies in combination with in vitro fertilization (IVF) in swine, and intracytoplasmic sperm injections (ICSI) in mouse, we have been able to implicate sperm-borne GSTO2 enzymes as constituents of nuclear decondensation and male pronuclear formation. Enzyme activity was inhibited through sperm pre-incubation with a membrane permeable inhibitor specific to the active site of GSTO enzymes prior to IVF or ICSI. These findings are also supported by additional IVF studies investigating GSTO involvement from the female perspective, fluorescent gel electrophoresis, and fluorescent immunocytochemistry experiments. Our findings suggest the absence of sperm-borne GSTO2 enzymes result in a developmental delay in pronuclear formation and ultimately cleavage in both swine and mouse, and implicates GSTO enzymes as important facilitators of successful nuclear decondensation and male pronuclear formation. This work was supported by NSERC (RGPIN/192093) (RO), Agriculture and Food Research Initiative Competitive Grant no. 2015-67015-23231 from the USDA National Institute of Food and Agriculture (PS), as well as by seed funding from the Food for the 21st Century Program of the University of Missouri (PS).

56. **NON-NUCLEAR CORE SOMATIC HISTONES ARE NOVEL CONSTITUENTS OF THE RAT PT AND APPEAR TO BE *DE NOVO* SYNTHESIZED DURING SPERMIOGENESIS.** Morgan Lion[1], Genevieve Acteau[1], Lauren Hamilton[1], Nicole Protopapas[1], Wei Xu[1], Peter Sutovsky[2,3], and Richard Oko[1], [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, [2]Division of Animal Sciences, College of Food, Agriculture and Natural Resources, and [3]Department of Obstetrics, Gynecology and Women's Health, School of Medicine, University of Missouri, Columbia, Missouri, USA

The perinuclear theca (PT) is a cytoskeletal structure that surrounds the spermatozoon nucleus and contains proteins involved in spermiogenesis and fertilization. Previously, we provided unprecedented evidence for the localization of non-nuclear core somatic histones within the bovine PT. Our current goal was to explore the extractability, localization, and developmental origin of core histones in the rat PT. SDS-PAGE analysis of SDS- or HCl-extracted rat PT-proteins revealed bands at 14kDa, 17kDa, 18kDa and 19kDa, corresponding to calf thymus core histones, H4, H2A, H2B, and H3, respectively. Immunofluorescent and immunogold labeling localized these histones to two PT sub-regions, the post-acrosomal sheath (PAS) and the murid-specific perforatorium (PERF). Early in development, the core histones are associated with the microtubular manchette of elongated spermatids; upon the manchette's descent, they appear to be deposited into the PAS and PERF. Since these PT sub-regions are formed at the end of elongation phase of spermiogenesis, following expulsion of the nuclear histones, we hypothesized that PT-derived histones are *de novo* synthesized in round spermatids. QRT-PCR analysis of mRNA from STAPUT-isolated testicular cells demonstrated that H2B expression was 2.6X higher in haploid cells than in tetraploid cells (when normalized to DNA content of respective cells). In summary, the non-nuclear core somatic histones reside in the PAS and PERF of murids, and may be synthesized *de novo* during spermiogenesis, rather than recycled from the nucleus. This work was supported by NSERC (RGPIN/192093) (RO), Agriculture and Food Research Initiative Competitive Grant no. 2015-67015-23231 from the USDA National Institute of Food and Agriculture (PS), as well as by seed funding from the Food for the 21st Century Program of the University of Missouri (PS).

57. **IL-13 AND IL-33 POLARIZE MACROPHAGES TO THE M2 PHENOTYPE AND CONTRIBUTE TO ENDOMETRIOSIS PATHOPHYSIOLOGY.** Ryan M. Marks[1], Jessica M. Miller[1], Vanessa R. Kay[1], Lindsey K. Symons[1], Asgerally T. Fazlebas[2], Chandra Tayade[1], [1]Department of Biomedical and Molecular Science, Queen's University, Kingston, ON Canada, [2]Obstetrics, Gynaecology and Reproductive Biology, Michigan State University, Lansing, MI USA

Endometriosis is a gynaecological disease characterized by the presence of extrauterine endometrial-like lesions. A dysfunctional immune response to refluxed menstrual effluents is indicated by aberrant peritoneal fluid cytokines and macrophage infiltration. Macrophages are innate regulators of angiogenesis, tissue repair, and inflammatory homeostasis. Evidence suggests that M1 (proinflammatory) and M2 (anti-inflammatory) macrophages are plastic cells with polarizable phenotypes regulated by local microenvironmental factors. M2 macrophages may facilitate lesion establishment at the mesothelial surfaces by promoting processes analogous to wound healing. IL-13 and IL-33 have been identified in the peritoneal fluid of women with endometriosis and have been demonstrated to synergistically polarize M2 macrophages in a variety of pathologies. *In vitro* evidence suggests that supernatants from macrophages treated with IL-13+33 synergistically promoted mesh formation in a HUVEC angiogenesis assay ($p<0.05$). Administration of IL-13 and IL-33 to our syngeneic mouse model of endometriosis produced peritoneal environment that is significantly increased cytokines involved in macrophage recruitment (GM-CSF, MCP-1), T_H2 (IL-4, IL-10) responses capable of polarizing M2 macrophages, and VEGF ($p<0.05$). IL-13+33 treated lesions appeared qualitatively larger and immunohistochemistry revealed increased proliferative (Ki-67) and vasculature (CD31) markers. These studies provide foundational evidence of a local peritoneal environment conducive to M2 polarization which may ultimately facilitate disease pathophysiology by promoting hallmarks of endometriotic lesion development.

58. **THE POST-ACROSOMAL SHEATH AND PERFORATORIAL REGIONS OF THE PERINUCLEAR THECA OF RAT SPERMATOZOA SHARE COMMON DEVELOPMENTAL ORIGINS AND PROTEIN CONSTITUENTS**. Nicole Protopapas[1], Lauren Hamilton[1], Wei Xu[1], Peter Sutovsky[2,3], and Richard Oko[1]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON, Canada, [2]Division of Animal Sciences, College of Food, Agriculture and Natural Resources, and [3]Department of Obstetrics, Gynecology and Women's Health, School of Medicine, University of Missouri, Columbia, Missouri, USA

The perinuclear theca (PT) is a dense cytosolic protein layer that surrounds the nucleus of the mammalian sperm head. It is divided into the subacrosomal layer (SAL) and the post-acrosomal sheath (PAS) in spatulate sperm, while in falciform-shaped sperm an additional apical region called the perforatorium emerges. The formation of the SAL and PAS vary, with the former assembling early in spermiogenesis concomitant with acrosome formation, and the latter dependent upon manchette descent during spermatid elongation. Commensurate with PAS development, perforiatorial proteins are also proposed to be transported by the manchette into their apical compartment. The similar means of assembly between the PAS and perforatorium suggest they share common protein constituents. This study investigated the compositional similarities and differences between the PAS and perforatorium using cell fractionation, immunoblotting and immunolocalization. Compositional analysis of the perforatorium identified a 15-kDa polypeptide (PERF15) as its major protein constituent. Further proteomic analysis of the PT localized several PAS-resident proteins including GSTO2, PAWP, WBP2 and the core somatic histones, to both the PAS and perforatorium. These findings support the developmental homogeny between the PAS and perforatorium, indicating a similar means of assembly between these regions of the PT. Taken together, the PT of falciform-shaped spermatozoa can be compositionally organized into three regions: the SAL, PAS, and perforatorium, with the latter two sharing similar protein constituents and developmental characterization. This work was supported by NSERC (RGPIN/192093) (RO), Agriculture and Food Research Initiative Competitive Grant no. 2015-67015-23231 from the USDA National Institute of Food and Agriculture (PS), as well as by seed funding from the Food for the 21st Century Program of the University of Missouri (PS).

59. **MECHANISMS OF CEREBRAL VASCULAR PATHOLOGY IN A NEW ANIMAL MODEL OF AGE-RELATED COGNITIVE IMPAIRMENT.** Ahmed M. Elharram, Rebecca D. Maciver, Mandy E. Turner, Michael A. Adams and Brian M. Bennett. Department of Biomedical and Molecular Sciences and Centre for Neuroscience Studies, Queen's University, Kingston Ontario Canada.

Oxidative stress causes tissue damage in a number of models of vascular cognitive impairment (VCI) and in age-related Alzheimer's disease (AD). We have developed a novel oxidative stress-based mouse model of age-related cognitive impairment based on gene deletion of aldehyde dehydrogenase 2 (ALDH2). ALDH2 is important for the detoxification of endogenous aldehydes such as 4-hydroxynonenal (HNE), a lipid peroxidation product formed during oxidative stress that can form protein adducts, altering cell function. $Aldh2^{-/-}$ mice exhibit oxidative stress, many AD-like pathologies, and age-related decreases in performance in recognition and spatial memory tasks beginning at 3 months of age and maximal at 6-7 months. Executive dysfunction, an early impairment seen in VCI, has also been exhibited in $Aldh2^{-/-}$ mice as demonstrated by a lack of reversal learning in the Morris Water Maze task. With respect to vascular pathologies, 9-12-month-old $Aldh2^{-/-}$ mice exhibit aortic endothelial dysfunction, and arterial hypercontractility, HNE adduct formation and age-related amyloid-β (Aβ) deposition in cerebral microvessels, loss of BBB integrity and cerebral vascular microbleeds. Echocardiographic analysis and radiotelemetry have also shown diastolic dysfunction, and elevated systolic, diastolic and mean arterial pressure at 12 months of age in male $Aldh2^{-/-}$ mice. A validated, oxidative stress-based animal model of cognitive impairment and age-related VCI will allow greater insight into the pathogenesis and molecular/cellular mechanisms of VCI.

60. **HIGH DOSE CALCITRIOL INDUCES VASCULAR CALCIFICATION IN NON-CKD RATS**. Corey M. Forster1, Mandy E. Turner1, Kimberly J. Laverty1, Emilie C. Ward1, Cynthia M. Pruss1, Rachel M. Holden2, Michael A. Adams1, 1Department of Biomedical and Molecular Sciences, Queen's University, Kingston ON, Canada, 2Department of Medicine, Queen's University, Kingston ON, Canada.

Premature mortality in chronic kidney disease (CKD) patients is linked to cardiovascular disease (CVD). In CKD, extra-osseous mineral deposition occurs, particularly vascular calcification (VC), causing a significant decline in vascular health. Calcium and phosphate homeostasis relies partially on 1,25-dihydroxvitamin D3 (calcitriol), parathyroid hormone (PTH), and fibroblast growth factor 23 (FGF-23). In CKD, renal calcitriol production declines generating secondary hyperparathyroidism, which is managed by administering vitamin D mimetics. However, vitamin D receptor activation can lead directly and/or indirectly to the development of VC. This study was designed to assess the temporal basis of calcitriol-induced VC in the absence of CKD, as the complex CKD phenotype can confound the profile of VC pathophysiology. Male Sprague-Dawley rats, aged 15-16 weeks, were randomly sorted into a subcutaneous (n=8) or an intraperitoneal injection group (n=5). Of these rats, one group received 1.0% dietary phosphate (n=10) while a second group received a 0.5% phosphate diet (n=3). After 72 hours, calcitriol was administered once daily (0.5 or 1 mg/kg). Daily blood samples were taken to monitor changes in biomarkers. At the end of the treatments, animals were sacrificed and tissues were collected to determine vascular mineral content, serum hormone levels, and vascular histology. Animals who received 8 doses, regardless or injection method, dose, or dietary phosphate developed VC, while animals who received 3 doses showed evidence of calcification in distal vessels. The mechanisms responsible for VC development have not been fully elucidated. Characterizing calcitriol-induced VC in the absence of CKD will enable insight into the mechanisms involved. (Supported by The Canadian Institutes of Health Research)

61. **INVESTIGATING PERTURBATIONS OF CD1 MOUSE FETAL TOPOISOMERASE IIA FOLLOWING BENZOQUINONE EXPOSURE.** Trent H. Holmes and Louise M. Winn. Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

Recent studies suggest that maternal exposure to benzene during fetal development may lead to leukemia (blood cancer) in offspring. While the etiology of fetal benzene-induced leukemia is unknown, benzene is known to affect the critical DNA repair enzyme topoisomerase IIα (TOP2a). To date no studies have investigated the effects of benzene on fetal TOP2a. The larger scope of this research will determine if and how benzene affects CD1 mouse fetal liver TOP2a, with the aim of this specific study to: (1) characterize cultured gestational day (GD) 14 fetal liver cells, (2) optimize detection of fetal TOP2A protein, and (3) measure specific fetal TOP2a activity. Flow cytometric analysis of GD14 fetal liver cell culture has shown both lymphoid and myeloid cells are present, supporting this model to determine how benzoquinone toxicity may affect blood cell development. To measure fetal TOP2a activity, cultured CD1 mouse fetal liver cells were exposed to 12.5 μM benzoquinone or PBS for 2, 12, and 24 hours. Fetal TOP2a activity was significantly decreased after 24 hours of benzoquinone exposure, but a change was not observed in 2 or 12 hour exposure. Ongoing studies are working towards the optimal detection of fetal TOP2a by Western blot. These experiments will help identify the role benzoquinone plays on fetal TOP2a. Support: CIHR

62. **ACUTE RESPONSE TO VITAMIN D TREATMENT IS ATTENUATED IN PROGRESSING EXPERIMENTAL CKD.** Lok Hang Lee[1], Mandy E. Turner[1], Emilie Ward[1], Kimberly J Laverty[1], Cynthia M. Pruss[1] , Rachel M. Holden[2], Michael A. Adams[1]; Biomedical and Molecular Sciences[1] and Department of Medicine[2], Queen's University, Kingston, ON, CANADA

Secondary hyperparathyroidism (SHPT), a risk factor for cardiovascular disease in chronic kidney disease (CKD) patients, is commonly treated with Vitamin D, but this treatment often fails. This study characterizes how single vitamin D doses (calcitriol) acutely suppress parathyroid hormone (PTH) as kidney function declines and dietary phosphate is increased in a dietary adenine rat model of CKD. In Sprague Dawley rats (N=10), a 0.25% adenine 0.5% phosphate diet was fed for 4.5 weeks to generate stable CKD. An oral calcitriol dose (160ng/kg) was given at baseline, 1, 3, and 5 weeks as CKD progressed with 0.5% dietary phosphate, and at 7 and 8 weeks on high (1.0%) dietary phosphate. Throughout CKD generation, the single dose of calcitriol consistently reduced PTH by 24 hours. The responsiveness was maintained despite elevations in PTH from 79.6±25.8 pg/mL to 221.4±66.7 by week 5. Following the increase in dietary phosphate, PTH increased to 1207±176 pg/mL to 1342±310, at 7 and 14 days high phosphate diet, respectively. PTH was no longer reduced at 24 hours following calcitriol dose at both time points, despite elevating serum calcium at 48 hours. This study shows that high dietary phosphate attenuates the suppression of PTH by an acute dose of calcitriol in stable experimental CKD. This supports the importance of limiting dietary phosphate in the CKD population to limit impact of PTH responsiveness and mineral bone disease in this population. Funding: CIHR.

63. **ASSESSMENT OF POSTNATAL CARDIAC STRUCTURE AND FUNCTION IN A SPRAGUE-DAWLEY MODEL OF CONGENITAL HEART DEFECTS.** Rebecca D. Maciver, Michael A. Adams, Louise M. Winn, & Terence R. S. Ozolinš., Department of Biomedical and Molecular Sciences, Queen's University, Kingston, ON.

Congenital heart defects (CHDs) are the most common birth defect, affecting approximately 1% of births. Clinically, 80% of CHDs spontaneously resolve by one year of age but are lost to follow up. We hypothesize these individuals may be predisposed to cardiovascular disease when exposed to stressors late in life, but this has not been clearly demonstrated. In order to test this hypothesis, we have developed a rat model in which dams are treated with dimethadione, a potent cardiac teratogen producing a 50% incidence of CHD. Previous studies have shown that these structural and functional defects resolve postnatally, and by adulthood DMO-exposed offspring are indistinguishable from unexposed cohorts, mimicking the clinical presentation of CHD. DMO exposure transiently reduces maternal food consumption and body weight gain so weight matched and *ad-libitum* control groups were included to eliminate confounding maternal nutritive status. Echocardiography was performed on male offspring on postnatal days (PND) 4, 21, 56, and 100 to assess cardiac structure and function longitudinally. We present altered trajectories of cardiac structural and functional development from neonate through adulthood under conditions of differential postnatal catch-up growth and *in utero* exposure to a heart teratogen. Additional studies conducted on these cohorts have used beta-adrenergic stimulation as a surrogate for cardiac stress to determine whether teratogen exposure and/or postnatal catch-up growth influences the maladaptive response of the heart in later life.

64. **ASSESSMENT AND REPORTING OF SAFETY OUTCOMES IN CLINICAL TRIALS OF CANNABINOIDS FOR CHRONIC PAIN.** Mohammed M. Mohiuddin, Ian Gilron, Simon Haroutounian, Shannon Smith, Fiona Campbell, Meg Carley. From the School of Medicine, Departments of Anesthesiology & Perioperative Medicine, Biomedical & Molecular Sciences, and Centre for Neuroscience Studies, Queen's University Kingston, Ontario Canada.

Chronic pain affects a significant proportion of the population and presents a major challenge to clinicians and pain specialists. Despite availability of treatment options such as opioids, chronic pain persists in patients, perhaps because of a lack of analgesic efficacy or poor tolerability from adverse effects. Cannabinoids present an alternative treatment option; however, it is unclear whether a clear profile of cannabinoid associated adverse events has been accurately detailed in the literature. A systematic review will be performed by searching for primary reports of double-blind randomized controlled trials of cannabinoids, compared to placebo, and any active comparator treatments studied, for chronic pain, with a primary outcome directly related to pain. The primary outcome will be the quality of adverse event reporting by the adherence of RCT's to CONSORT Extensions for Harms recommendations. Secondary outcomes will be: type of adverse event, method of adverse event reporting, timing of adverse assessment reporting, severity of adverse events, patient withdrawals and reasons for patient withdrawals. A descriptive approach to data analysis and reporting will be used. The percentage of trials fulfilling each CONSORT Extension for Harms recommendation, and the number of recommendations fulfilled by each trial will be recorded. Ultimately, this project seeks to promote the safety of patients in whom cannabinoids reduce chronic pain and improve quality of life, by reducing undesirable side effects, and preventing serious harms.

65. **MEAL PHOSPHATE BIOAVAILABILITY ALTERS HORMONAL RESPONSE IN HEALTHY HUMANS.** Kathryn Neville, Mandy E Turner, Nicole Couture, Laura Couture, Cynthia M Pruss, Michael A Adams, Rachel M Holden**,** Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario Canada

Background: Chronic kidney disease (CKD) patients have impaired phosphate excretion, leading to chronically elevated parathyroid hormone (PTH) and eventually hyperphosphatemia. Elevated phosphate and PTH contribute to mineral-bone disorders and cardiovascular disease. Dietary phosphate contributes to the elevation of these biomarkers, therefore CKD patients are often prescribed phosphate-restricted diets. Current guidelines place little emphasis on the composition of sources, however phosphate sources vary greatly in their bioavailability. **Methods**: Healthy individuals (N=18) were recruited. Two meals with identical phosphate amounts, but different compositions were selected; one healthy meal containing organic phosphate sources, and a second convenience-style meal with inorganic phosphate sources. Fasted participants were randomized to one of the meals. Baseline urine and blood samples were taken before meal consumption. Post-prandial blood and urine samples were taken over three hours. Participants returned to consume the second meal at least seven days later. **Results**: Compared to the convenience meal, the healthy meal displayed significantly lower serum and urinary phosphate, significantly increased serum calcium, and significantly decreased serum PTH. Urinary calcium levels were not significantly different between meals. Preliminary results in CKD patients show similar trends. **Conclusions**: Differences in mineral and hormonal responses between meals can likely be attributed to the meals' bioavailability, although insulin response could also have a role. These data suggest that dietary restrictions should discriminate the phosphate bioavailability and composition, in addition to amount. (Supported by Queen's University Department of Medicine)

66. **CHARACTERIZING THE EFFECTS OF IN UTERO EXPOSURE TO VALPROIC ACID ON FETAL HEART DEVELOPMENT.** Ana Nikolovska, Louise Winn**,** Department of Biomedical and Molecular Sciences, Queen's University Kingston, Ontario Canada.

Many of the antiepileptic drugs (AEDs) currently on the market have a wide range of therapeutic effects in addition to treating epilepsy, however, studies have shown that *in utero* exposure to AEDs, particularly valproic acid (VPA), can have detrimental effects on embryonic development. Specifically, *in utero* exposure to VPA has been associated with a higher risk of congenital heart defects. In spite of this, expectant mothers are advised to continue treatment throughout pregnancy to prevent seizures, which can lead to physical injury as well as oxygen deprivation to the fetus. To characterize the effects of VPA, pregnant CD-1 mice were dosed with 400mg/kg of VPA on gestational day (GD) 9, and ultrasounds were performed on GD 14 to 18 prior to harvesting the fetal hearts on GD19. Using high-resolution ultrasound technology, we can observe the effects of VPA on cardiac contractility, followed by histology to characterize the effects of VPA on myocardial organization and left ventricular diameter. We expect to see a decrease in contractility in the VPA exposed fetal mice when compared to control group. Using H&E staining to visualize the structure of the heart, as well as Masson's Trichrome staining to identify collagen deposition, we expect to see enlarged left ventricular diameter and disrupted myocardial organization.

67. **MAGNESIUM FOR THE MANAGEMENT OF CHRONIC PAIN: A SYSTEMATIC REVIEW AND META-ANALYSIS.** Rex Park, BHSc, Ian Gilron, MD, MSc, FRCPC, Anthony Ho, MD, FRCPC, Meg Carley, BSc. From the School of Medicine, Departments of Anesthesiology & Perioperative Medicine, Biomedical & Molecular Sciences, and Centre for Neuroscience Studies, Queen's University, Kingston, Ontario, Canada.

Chronic pain is one of the most common reasons for medical visits and is estimated to affect 1.5 billion people worldwide. Chronic pain is associated with increased mortality and has major negative impacts on daily living activities and work-related outcomes, such as employment status and productivity. The direct health care and productivity costs of chronic pain is as high as $635 billion per year in the US, which exceed the annual costs from cancer and heart disease. Despite the variety of treatments available, they have limited efficacy and dose-limiting adverse effects, leaving a significant unmet need for sufferers. Recent increases in opioid use for chronic pain have been associated with rising opioid-related mortality and other serious problems, emphasizing the need for better nonopioid therapies. Magnesium is a blocker of the NMDA receptor, which is critical in the transmission of pain. Through this mechanism, magnesium administration may prevent nociceptive-associated central sensitization and dampen the activity of the dorsal horn neurons, ultimately reducing the pain experience. Emerging evidence supports the safe use of magnesium in controlling chronic pain, but there is no consensus regarding its clinical efficacy. With our background with the Cochrane Collaboration and experience with several previous systematic reviews, we will implement a systematic literature search strategy to synthesize and, where appropriate, conduct meta-analyses of clinical trials of magnesium for the treatment of chronic pain.

68. **ALTERATION IN MICRO-RNA EXPRESSION PATTERN IN CD-1 MOUSE FETAL LIVER CELLS FOLLOWING IN-VITRO BENZOQUINONE EXPOSURE.** Alexander Platt[1], Louise M. Winn[1,2], [1]Department of Biomedical and Molecular Sciences, Therapeutics, Drug Development and Human Toxicology Graduate Field Queen's University, Kingston, Ontario, Canada, [2]School of Environmental Studies, Queen's University, Kingston, Ontario, Canada

Background:Benzene is a ubiquitous environmental pollutant associated with the occurrence of childhood leukemia. While the mechanism of benzene's transplacental carcinogenicity is not fully understood, the expression pattern of micro-RNAs (miRs) may be altered. miRs are single-stranded fragments of RNA found naturally in the cell that regulate gene expression by binding to complementary mRNA sequences. miRs have essential roles in a wide range of physiological and pathological processes, including normal hematopoiesis and hematopoietic malignancies, such as leukemia. Objectives: The aim of this study was to identify expression patterns of miRs in CD-1 mouse fetal liver cells, and determine whether exposure to BQ alters the expression pattern of specific miRs associated with leukemia. Methods: Cultured fetal liver cells were exposed to 12.5 μM BQ or PBS for 3, 6, or 24 h. miR expression profiles were assessed with a hybridization plate array followed by verification of specific miR levels (miR-146a, 155, and 19b) via qRT-PCR. Results: BQ exposure demonstrates a variation in miR expression pattern in hematopoietic cells. A nonsignificant increase in the mRNA expression of miR-146a and miR-155 was further validated compared to PBS controls. Conclusions: These studies suggest the involvement of miRs may play a mechanistic role in benzene induced leukemogenesis. Initial results justify further studies involving benzene initiated leukemogenesis and miRs.

69. **INVESTIGATING THE EFFECTS OF VALPROIC ACID EXPOSURE ON PLACENTAL GROWTH AND FETAL DEVELOPMENT DURING EARLY PREGNANCY IN CD1 MICE.** *Sidra Shafique[1], Louise M. Winn[1,2].Department of Biomedical and Molecular Sciences, Queen's University, Kingston[1], School of Environmental Studies, Queen's University, Kingston[2]*

Valproic acid (VPA) is an effective anti-epileptic drug used to treat seizures, bipolar disorders and neuropathic pain in reproductive aged women. VPA crosses the placental barrier and induces birth defects in the developing fetus. Literature indicates VPA adversely affects fetal growth but fails to inform on the association of fetal and placental growth at the same time. We hypothesized that the fetal growth restriction by *in vivo* VPA exposure is associated with reduced placental weight. Pregnant CD-1 dams were exposed to a single dose of 400mg/kg VPA or the vehicle control via subcutaneous injection on gestational day (GD) 9 and fetuses were harvested on GD 13, 15, 17 and 19 respectively. Resorptions and external deformities, fetal crown-rump length (CRL), fetal weight, placental weight, placental diameter were measured. There was a significant increase ($p<0.05$) in the frequency of exencephaly in treated group. Results indicated a non-significant trend of reduction in fetal and placental weight in VPA treated, in both non-affected and exencephalic treated groups. The data indicates that *in utero* VPA exposure may decrease fetal and placental weight in visually non-affected and exencephalic VPA-exposed fetuses. [Funding: CIHR]

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70. **VASCULAR OUTCOMES OF A PREGNANCY COMPLICATED BY PREECLAMPSIA.** Logan C Barr, Julia Herr, Claire Sumner, Jessica Pudwell, Amer M Johri, Graeme N Smith. Kingston Health Sciences Centre, Queen's University.

Background Pre-eclampsia (PE) is a maternal hypertensive disorder associated with elevated lifetime risk for cardiovascular disease (CVD), and we hypothesize that microvascular dysfunction following PE precedes these changes. The objective of this study is to use laser speckle contrast imaging (LSCI) to determine the extent to which PE is associated with microvascular endothelial changes postpartum, and its correlation to macrovascular indicators of health. **Methods/Results** Healthy women with previous PE (n=6) and normotensive controls (n=6) between 6 months and 5 years postpartum were recruited. Microvascular reactivity in the right volar forearm was assessed using LSCI coupled with iontophoresis of 1% acetylcholine (Ach) and sodium nitroprusside (SNP) solutions. Carotid intima media thickness (CIMT), plaque burden, and carotid strain were assessed with a two-dimensional carotid ultrasound scan. Vasodilation significantly increased in a dose-response fashion with iontophoresis of both Ach and SNP for both groups ($P<0.05$). There was a significant difference ($P<0.05$) between preeclamptic and normotensive women only for the endothelial-dependent (ie. Ach) vasodilation. There were no significant differences between subject groups in sodium nitroprusside-mediated vasodilation. No differences between normotensive and preeclamptic participants were found for CIMT, plaque burden, or strain. **Conclusions** PE is associated with increased endothelium-dependent microvascular reactivity. Ongoing recruitment will elucidate the precise relationship of PE and the microvasculature. Similarities in macrovascular health indicators between subject groups corroborate our hypothesis that microvascular dysfunction predates later-life CVD.

71. **THE EFFECT OF IN UTERO BENZENE EXPOSURE ON FETAL NF-κB CELL SIGNALLING IN CD-1 MICE.** Peter Chun Wan Lu, Louise Winn, DBMS.

In utero exposure to benzene, a known carcinogenic environmental toxicant, is associated with the development of childhood leukemia. We have previously demonstrated that *in utero* exposure to benzene in CD-1 mice can alter the expression of transcription factor NF-κB, which regulates genes involved in cell proliferation and programmed cell death, however, a full characterization of benzene's effects on fetal NF-κB is still needed. Since NF-κB regulates genes involved in cell proliferation, inappropriate activation can result in the proliferation of damaged cells potentially leading to the development of childhood leukemia. We hypothesize that benzene metabolism in the maternal liver produces reactive oxygen species that leads to fetal changes in NF-κB signalling. To test this hypothesis, pregnant CD-1 mice were exposed to 200 mg/kg benzene or its vehicle control on gestational days 8, 10, 12, and 14. Dams were sacrificed at 2, 4, and 24 hours after the last benzene dose. Fetal livers were collected, and immunoblotting was done to assess changes in protein levels of phospho-p65 (Ser276). Preliminary results showed that after *in utero* benzene exposure, protein levels of phospho-p65 (Ser276) significantly decreased at 2 and 6 hours after the last benzene dose. Future steps will assess DNA binding activity of phospho-p65 (Ser276) along with levels and activity of other proteins involved in the NF-κB signalling pathway. Canadian Institutes of Health Research (CIHR)

72. **CARBON MONOXIDE ALTERS ENDOTHELIAL FUNCTION IN PERIPHERAL MICROVASCULATURE.** Karalyn E McRae[1], Jessica Pudwell[2], Nichole Peterson[1], and Graeme N Smith[1,2]. [1]Department of Biomedical and Molecular Sciences, Queen's University, Kingston, Ontario, Canada and [2]Department of Obstetrics and Gynecology, Queen's University, Kingston, Ontario, Canada.

Introduction: Pre-eclampsia (PE) is characterized by maternal endothelial dysfunction. Measuring endothelial reactivity in the microvasculature could identify women with underlying endothelial sensitivity. Carbon monoxide (CO) is a vasodilator that may improve endothelial function and have promise as a novel therapeutic. **Objectives**: To quantify changes in microvascular vasodilation during exposure to low dose CO. **Study Methods:** Non-pregnant women inhaled 250ppm CO for a 24-min period. Microvascular flux was measured in the forearm using MoorFLP-2 Laser Speckle Contrast Imaging. Flux was recorded for a 10-min baseline followed by a 3 min arterial occlusion to measure microvascular response to post-occlusive reactive hyperemia (PORH). Data is presented as the difference in Max Level/Resting Level and ML/Baseline Zero ratios and time to half-recovery (TH). PORH data was analyzed by unpaired t-test. TH is presented as a survival curve and analyzed by Cox-Proportional Hazard Ratios and 95% Confidence Intervals (CI). Analysis by GraphPad Prism v6.0 or SPSS with a significance of $p<0.05$. **Results:** Participant demographics were similar across all groups. CO increased both the difference of ML/RL ratio (0.532 ± 0.442 vs. -0.056 ± 0.388, $p<0.05$) and ML/BZ ratio (0.413 ± 0.526 vs, -0.775 ± 0.791, $p<0.05$). CO increased TH compared to controls (Cox-Proportional Hazard Ratio 0.17, 95% CI =0.03-0.96, $p=0.045$). **Conclusions:** This study demonstrated that CO increased microvascular vasodilation and suggests that CO may help attenuate endothelial dysfunction in PE. **Funding:** CIHR Catalyst Grant (GNS), Ontario Graduate Scholarship (KEM).